09/278,601

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

STEPHEN CHARLES INGLIS, MICHAEL EDWARD GRIFFITH BOURSNELL and ANTHONY CHARLES MINSON,

Junior Party,
(Patents 5,665,362 and 5,837,261)

v.

DAVID KNIPE, ROBERT FINBERG and GEORGE SIBER,

Senior Party,
(Application 08/278,601)

Patent Interference No. 104,363

Before: McKELVEY, Senior Administrative Patent Judge, and SCHAFER and SPIEGEL, Administrative Patent Judges.

SPIEGEL, Administrative Patent Judge.

MEMORANDUM OPINION and ORDER
(Decision on preliminary and other miscellaneous motions)

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1. MICROBIOLOGY: AN INTRODUCTION, Tortora et al., The Benjamin/Cummings Publishing Company, Inc., Menlo Park (1982), pages 396-398, 423-424 and 735.

2. MICROBIOLOGY, third ed., B. Davis et al., eds., Harper & Row Publishers, Hagerstown (1980), page 294.

3. ILLUSTRATED DICTIONARY OF IMMUNOLOGY, J. Cruse et al., eds., CRC Press, Boca Raton (1995), pages 121, 134-135 and 309.

4. MOLECULAR BIOLOGY AND BIOTECHNOLOGY, R. Meyers, ed., VCH Publishers, Inc., New York, NY (1995), pages 367-368.

5. FUNDAMENTAL VIROLOGY, second edition, B. Fields et al., eds., Raven Press, Ltd., New York, NY (1991), pages 87-94 and 849-895.

6. FUNDAMENTAL VIROLOGY, third edition, B. Fields et al., eds., Raven Press, Ltd., New York, NY (1993), pages 837-863.

A. Introduction

This is a decision on preliminary and miscellaneous motions filed by parties Inglis and Knipe in Interference 104,363.

Neither party requested oral argument.

B. Background Technology Discussion

1. General comments

a. introduction

The interference involves viral vaccines. The following is our understanding of the subject matter involved in the interference.

b. specific immune responses

When a microorganism or antigen, such as a virus, invades a body, e.g., through the mouth, the nose or a break in the skin, the body mounts a specific defense against the invader. If virus A invades the body, A antibodies are produced; if virus B invades the body, B antibodies are produced; and so on. These specific antibodies and other specific defenses against the invading virus are produced by the immune system and provide the body with a resistance to disease caused by the invading virus. This specific resistance is called immunity.

The immune system has two parts. Both parts involve body cells called "lymphocytes." "Humoral" immunity involves lymphocytes, called "B cells," which make antibodies that are then secreted into body fluids or "humors," e.g., blood. "Cell-mediated" immunity involves lymphocytes, called "T cells," which make antibodylike

molecules that remain attached to the surface of the T cell. The humoral immune response primarily defends against invaders, e.g., bacteria and viruses, present in body fluids. The cell-mediated immune response primarily defends against invaders, e.g. intracellular viruses, present in cells. The particular protection provided by each type of response overlaps.

Immunity is also divided into "native" and "acquired" immunity. "Native" immunity is the resistance to disease that is present at birth. For example, humans have "native" immunity against canine distemper and hog cholera. "Acquired" immunity is the ability, obtained during the lifetime of an individual, to produce specific antibodies in response to an antigen.

"Acquired" immunity can be "naturally" acquired or "artificially" acquired. "Naturally" acquired immunity occurs when the individual comes in contact with the antigen by natural processes such as infection. The individual actively produces antibodies against the antigen. Sometimes the immunity lasts a lifetime, as with chickenpox; other times the immunity only lasts a few years, as with tetanus. "Artificially" acquired immunity occurs when a carefully chosen antigen is deliberately introduced into the body in a vaccine preparation to stimulate antibody production against the specific antigen. For example, vaccines are available against the microorganisms that produce polio, whooping cough, smallpox, rabies and influenza. Vaccination involves both humoral and cell-mediated immune responses, i.e., both antibody production and T cell immunity. Vaccination is an important medical

intervention for preventing disease. (See Tortora[1], pp. 396-398; Ex 2011, p. 2, ll. 14-15; Davis,[2] page 294; Cruse[3], p. 309; Meyers[4], pp. 367-68.)

c. traditional vaccines

Traditional vaccines against disease caused by viruses are based on killed or live but attenuated (weakened) viruses that can stimulate a specific immune response to the virus. Ideally, the vaccine virus is altered to the point that it will not produce the signs and symptoms of the disease but is still able to stimulate antibody formation against that specific disease. However, using either killed or live attenuated viruses has certain disadvantages.

Killed virus vaccines stimulate the production of antibodies against viral coat or envelope proteins. The use of chemicals or heat to kill a virus may alter important surface structures of the virus. Since immunity is induced against the "altered" virus, the antibody may not be as reactive with the natural form of the viral coat or envelop protein. In addition, the antibodies may only last in the body fluids for several months. Finally, extreme care must be exercised to assure that no live virus is present in the vaccine.

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[1] MICROBIOLOGY: AN INTRODUCTION, Tortora et al., The Benjamin/Cummings Publishing Company, Inc., Menlo Park (1982).

[2] MICROBIOLOGY, third ed., B. Davis et al., eds., Harper & Row Publishers, Hagerstown (1980).

[3] ILLUSTRATED DICTIONARY OF IMMUNOLOGY, J. Cruse et al., eds., CRC Press, Boca Raton (1995).

[4] MOLECULAR BIOLOGY AND BIOTECHNOLOGY, R. Meyers, ed., VCH Publishers, Inc., New York, NY (1995).

Attenuated viruses are typically prepared by culturing and serially reculturing the virus through chick embryo or tissue culture cell lines until the virus has lost its disease-causing ability or "virulence." These live but "weakened" viruses have the advantage of acting like a natural infection, e.g., they multiply in the host and produce longer lasting immunity because the immune system is constantly stimulated. However, there may be contaminants present in the culture system which may cause problems in the vaccinee. Further, some live viral preparation are unstable and may actually lose infectivity during storage. On the other hand, there is a risk that the attenuated virus may revert to a form showing even greater virulence when it multiplies within the vaccinee, in which case the vaccine would make the vaccinee even sicker than the live virus. (See Ex 2003, col. 1, ll. 10-60; Tortora, pp. 423-24; Meyers, p. 368.)

d. subject matter of the interference

Biotechnology has led to the production of genetically engineered vaccine preparations. These vaccines are based on "mutant" viruses.

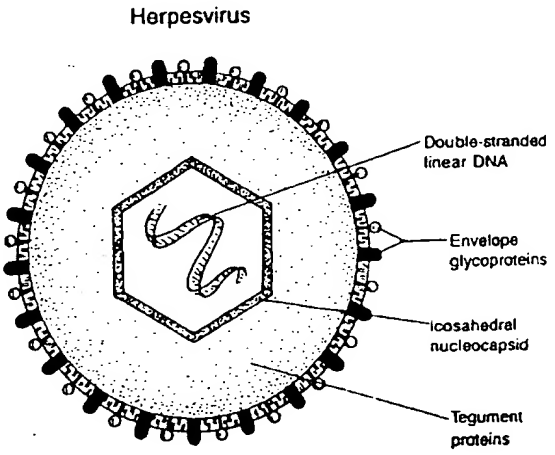
All the genetic information in most cells is contained in its nucleic acid or "genome." A gene is a segment of nucleic acid that codes for a functional product. It is possible to "delete" or "inactivate" a gene from a viral genome, i.e., to produce a mutant virus, and to provide a recombinant "complementing" host cell which provides the virus with the product of the deleted or inactivated gene. The mutant virus grows well on the complementing cell but not a normal host cell. (See Tortora, p. 735; Cruse, p. 121; Ex 2003, col. 2, ll. 5-18.)

A viral vaccine based on a mutated virus, like a viral vaccine based on a live, attenuated virus, can act like a natural infection with regard to its effect on immunity. However, unlike a live, attenuated viral vaccine, a vaccine based on a mutated virus can be prevented from multiplying within a normal host cell and/or producing progeny virus which is capable of infecting new normal host cells. Exactly how much like a natural infection the mutated virus acts or what kind of "progeny" it makes in the infected host cell depends upon where the mutation occurs in the viral genome.

The subject matter of the interference involves vaccines based on herpesvirus mutants wherein a herpesvirus gene encoding a protein essential for replication of the herpesvirus is deleted or inactivated such that the mutated virus can grow in a "complementing" host cell, but not in a normal host cell. The mutated viral vaccine maintains advantages of live viral vaccines while overcoming many of the safety disadvantages inherent in the use of live viral vaccines.

2. Herpesvirusreplication and infection

a. the normal structure of a herpesvirus [*Figure* taken from Cruse, p. 134.]



Herpesvirus contains a central core of double-stranded DNA, also called its "genome." The DNA is surrounded by a protein coat called a "capsid." The capsid is covered by an "envelope" made of glycoproteins. In addition, herpesviruses have a space between the capsid and the envelope, called the "tegument," which also contains some viral proteins.

A "nucleocapsid" is the capsid together with the enclosed DNA.

A "virion" is the complete infectious virus particle which, in the case of herpesvirus, includes the nucleocapsid plus the surrounding tegument and envelope. (See generally, Cruse pp. 134-135).

b. infection

Whether a virus infects a particular host cell depends upon the requirements for specific attachment of the virus to the host cell and the availability of host cellular factors required for viral multiplication. Multiplication is not by growth and division but by production of virus parts and their subsequent assembly. Multiplication of enveloped viruses, e.g., herpesvirus, typically involves (1) attachment, (2) penetration, (3) biosynthesis of viral components, e.g., capsids and DNA, (4) maturation, including assembly of virions, and (5) lysis of the host cell and release of new virions.

The ability of a virus to multiply and the fate of the infected cell hinge on the synthesis and function of virus gene products, i.e., viral proteins. Viral proteins ensure the replication of the viral genome, the packaging of the genome into virions and alter the structure and /or function of the infected cell. Some viral proteins perform multiple

functions.

(1) attachment

Attachment is the specific binding of a virion protein ("anti-receptor") to complementary sites on the host cell surface ("receptor"). These "anti-receptors" are usually glycoproteins, i.e., proteins with pendant sugar groups. At a minimum, glycoproteins gB, gD and gH represent the minimum set of surface envelop proteins necessary for herpesvirus attachment and penetration.

Mutations in genes expressing antireceptors, e.g., gH, may cause the virus to lose its capacity to interact with certain receptors, i.e., to lose its ability to infect the host cell.

(2) penetration

Penetration of enveloped viruses occurs by fusion of the envelope. The de-enveloped nucleocapsid is transported to the host cell nucleus, where DNA is released into the nucleus.

(3) biosynthesis of viral components

Herpesviruses encode many proteins involved in the synthesis of viral DNA. The synthesis of viral gene products is tightly regulated. Viral gene expression is coordinately regulated and sequentially ordered in a cascade fashion.

A portion of the viral DNA, the "early" genes, is transcribed, i.e., specific mRNA is synthesized from this viral DNA. The mRNA is then translated to synthesize virus-specific proteins, e.g., enzymes required for DNA synthesis. Host cell DNA synthesis is

temporarily elevated and then suppressed as the host cell shifts over to the manufacture of viral DNA. Sometime later, transcription and translation of the remaining "late" viral genes occur, leading to synthesis of capsid proteins, which occurs in the cytoplasm of the host cell. The capsid proteins migrate into the nucleus of the host cell where maturation occurs.

Mutations in "late" genes, e.g., may result in no progeny virus being produced because a viral component, e.g., the capsid, required to assemble the progeny virus was not synthesized.

(4) maturation

Maturation is usually a spontaneous process and starts with the assembly of the nucleocapsid in the nucleus of the host cell. The envelop protein of herpesvirus is synthesized by the virus and is incorporated into the nuclear membrane of the host cell. The nucleocapsid assembly pushes through the nuclear membrane. As a result a portion of the nuclear membrane of the host cell, now the envelope, adheres to the virus. The virus particle is then transported from the vicinity of the nucleus to the exterior of the host cell.

(5) host cell lysis with release of progeny virus

The infected host cell usually dies as a result of the accumulation of large numbers of multiplying viruses, by the effects of viral proteins on host cell plasma permeability, or by inhibition of host DNA, RNA or protein synthesis.

(See generally, Fields[5], pp. 87-94, 847-856; Cruse, pp. 134-35.)

3. Herpesvirus genes and timing of their expression

The herpesvirus genome encodes about 80 viral proteins. Purified herpesvirus virions contain approximately 33 proteins. The remaining proteins include a large number of enzymes involved in viral DNA replication.

Herpesvirus genes are categorized into three major groups, i.e., immediate-early, early and late. Immediate-early or "α" genes are the first to be expressed. They encode five regulatory proteins, i.e., infected cell polypeptides (ICPs) 0, 4, 22, 27 and 47. Upon infection, the transcription of these genes is activated by a protein present on incoming virion. They do not require any prior viral protein synthesis. Early or "β" genes are not expressed in the absence of the immediate-early proteins. These genes encode enzymes, e.g., viral thymidine kinase and DNA polymerase. The appearance of early proteins signals the onset of viral DNA synthesis. The remaining genes, the late or γ genes, encode structural proteins, such as capsid protein and surface glycoproteins B and D. Expression of the late genes requires the presence of functional immediate-early proteins. (See generally, Fields, pp. 857, 861.)

4. Classes of immunoglobulins

Antibodies are immunoglobulins (Igs) of defined specificity produced by plasma or B cells. Mouse, rat and human all have five main classes or isotypes of immunoglobulins: IgM, IgD, IgG, IgA and IgE. Each of these mammalian species also

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[5] FUNDAMENTAL VIROLOGY, second edition, B. Fields et al., eds., Raven Press, Ltd., New York, NY (1991).

produce subclasses of Ig. Mice produce IgG1, IgG2a, IgG2b and IgG3. Rats produce IgG1, IgG2a, IgG2b and IgG2c. Humans produce IgG1, IgG2, IgG3 and IgG4, as well as IgA1 and IgA2.

The first antibodies produced in response to an antigen challenge are primarily of the IgM class. IgG, IgA and IgE class antibodies are produced later, but account for most of the antibody that is produced during a memory response. A memory response is produced by memory cells. Memory cells are T and B cells that can mount an accentuated immune response to an antigen, because of their previous exposure to that antigen through infection or immunization.

The subsequent immune response that switches from secretion of an IgM isotype to other isotypes of immunoglobulins is controlled by the antigens used for immunization and different cell factors. Different IgG subclasses are produced in response to different antigenic challenges. Soluble protein antigens primarily stimulate an IgG1 response in mice, while carbohydrate antigens induce a substantial IgG3 response, IgG2c response in rats and IgG2 responses in humans. Viruses mostly induce IgG2a responses in mice, and IgG1 and IgG3 responses in humans. Mouse IgG2a responses are regulated by cell factors produced by T cells, including interferon gamma (IFN-γ) and interleukin 4 (IL-4). IFN-γ induces IgG2a production and IL-4 suppressed IgG2a production.

The functional properties of particular IgG subclasses appear to make them particularly well suited to binding or destroying particular types of antigen or pathogen.

For example, mouse IgG2a is particularly well suited to the control of viral and gram-negative bacteria infections. (See generally, Fields (3d ed.), pp. 837-846.)

C. Findings of fact

The following findings of fact are supported by a preponderance of the evidence.

Junior party

1. The junior party is Stephen Charles Inglis, Michael Edward Griffith Boursnell and Anthony Charles Minson (**Inglis**).

2. Inglis is involved in the interference on the basis of U.S. Patent 5,837,261, granted November 17, 1998, based on application 08/216,260, filed March 21, 1994.

3. Inglis patent '261 has been accorded benefit for the purpose of priority of

U.S. application 08/168,643, filed December 16, 1993,

U.S. application 08/030,073, filed May 20, 1993,

British application 9324964.7, filed December 6, 1993,

British application 935710.7, filed March 19, 1993, and

British application 9226127.6 filed December 1992

(see Paper 1, p. 45).

4. Inglis is also involved in the interference on the basis of U.S. Patent 5,665,362, granted September 9, 1997, based on application 08/384,963, filed February 7, 1995.

5. Inglis patent '362 has been accorded benefit for the purpose of priority of

U.S. application 08/030,073, filed May 20, 1993

(see Paper 1, p. 46).

6. The real party in interest is Cantab Pharmaceuticals Research Limited.

Senior party

7. The senior party is David Knipe, Robert Finberg and George Siber (**Knipe**).

8. Knipe is involved on the basis of application 08/278,601, filed July 21, 1994 (Ex 2011).

9. Knipe application 08/278,601 has been accorded benefit for the purpose of priority of

U.S. application 08/179,106, filed January 10, 1994 and

U.S. application 07/922,912, filed July 31, 1992

(see Paper 1, p. 47).

10. The real party in interest is Dana-Farber Cancer Institute and The President and Fellows of Harvard College.

The interference

11. The subject matter in interference is defined by one count.

12. Count 1 (Paper 1, p. 48) reads:

Count 1

A composition according to claim 1 of Inglis '261 or any of claims 1 or 24 of Inglis '362 or any of claims 1, 5, 9, 25, 42-45 of Knipe

or

a method according to any of claims 20, 24 or 41 of Inglis '261 or claim 13 of Inglis '362

or any of claims 12, 17, 18, 32 or 37 of Knipe.

13. Inglis '261 composition claim 1 reads:

A pharmaceutical which comprises an infectious virus, said infectious virus consisting essentially of an effective immunizing amount of a mutant viral gene, said viral gene being essential for the production of infectious new virus particles, wherein said mutant herpesvirus[6] is able to cause production of infectious new virus in a recombinant complementing host cell expressing a gene which complements said essential viral gene, but is unable to cause production of infectious new virus particles when said mutant virus infects a host cell other than said recombinant complementing host cell, for prophylactic or therapeutic use in generating an immune response in a subject infected therewith.

14. Inglis '362 composition claim 1 reads:

A vaccine comprising a pharmaceutically acceptable excipient and an effective immunizing amount of a mutant herpesvirus, said mutant herpesvirus containing a genome in which a viral gene encoding a protein which is essential for production of infectious virus has been deleted or inactivated, wherein said mutant virus is able to cause production of infectious new virus particles in a recombinant complementing host cell expressing a gene which complements said essential vital gene,[7] but is unable to

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[6] There is no explicit antecedent support for "said mutant herpesvirus." We are construing "said infectious virus" as providing implicit antecedent support of "said mutant herpesvirus."

[7] There is no explicit antecedent support for "said essential vital gene." We are construing "a viral gene encoding a protein which is essential for production of infectious virus" as providing implicit antecedent support for "said essential vital gene."

cause production of infectious new virus particles when said mutant virus infects a host cell for prophylactic or therapeutic use in generating an immune response in a subject infected therewith.

15. Inglis '362 composition claim 24 reads:

A vaccine comprising a pharmaceutically acceptable excipient and an effective immunizing mount [sic, amount] of an infectious virus, wherein the infectious virus in said vaccine consists essentially of a mutant herpesvirus containing a genome in which a viral gene encoding a protein which is essential for production of infectious virus has been deleted or inactivated, wherein said mutant virus is able to cause production of infectious new virus particles in a recombinant complementing host cell expressing a gene which complements said essential viral gene, but is unable to cause production of infectious new virus particles when said mutant virus infects a host cell other than said recombinant complementing host cell, for prophylactic or therapeutic use in generating an immune response in a subject infected therewith.

16. Knipe composition claim 1 reads:

A pharmaceutical composition comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect an antibody subclass shift of IgG2a/IgG upon in vivo administration to a mammal.

17. Knipe composition claim 5 reads:

A pharmaceutical composition comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to induce production of IFN-γ upon administration to a mammal.

18. Knipe composition claim 9 reads:

A pharmaceutical composition comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to induce an immunological protective effect upon administration to a mammal.

19. Knipe composition claim 25 reads:

A vaccine in a pharmaceutically acceptable carrier comprising a mutated herpesvirus capable of infecting a mammalian cell and of eliciting a protective immune response in a mammal vaccinated with said herpesvirus, said herpesvirus being characterized by a mutation in at least one gene encoding a protein essential for replication of said herpesvirus, said mutation rendering said virus replication defective with the proviso that the herpesvirus is not a gH deletion mutant.

20. Knipe composition claim 42 reads:

A vaccine comprising a pharmaceutically acceptable carrier and an amount of a mutant herpesvirus effective to elicit a protective immune response, said mutant

herpesvirus containing a genome in which a viral gene encoding a protein which is essential for production of infectious virus has been deleted or inactivated, wherein said mutant virus is able to cause production of infectious new virus particles in a recombinant complementing host cell expressing a gene which complements said essential viral gene, but is unable to cause production of infectious new virus particles when said mutant virus infects a host cell other than said recombinant complementing host cell, for prophylactic or therapeutic use in generating an immune response in a subject infected therewith.

21. Knipe composition claim 43 reads:

A vaccine comprising a pharmaceutically acceptable carrier and an amount of a mutant herpesvirus effective to elicit a protective immune response, said mutant herpesvirus containing a genome in which a viral gene encoding a protein which is essential for production of virus has been deleted or inactivated, wherein said mutant virus is able to cause production of new virus particles in a recombinant complementing host cell expressing a gene which complements said essential viral gene, but is unable to cause production of new virus particles when said mutant virus infects a host cell other than said recombinant complementing host cell, for prophylactic or therapeutic use in generating an immune response in a subject infected therewith.

22. Knipe composition claim 44 reads:

A vaccine comprising a pharmaceutically acceptable carrier and an amount of a mutant herpesvirus effective to elicit a protective immune response, said mutant

herpesvirus containing a genome in which a viral gene encoding a protein which is essential for replication of the virus has been deleted or inactivated, wherein said mutant virus is able to cause production of new virus particles in a recombinant complementing host cell expressing a gene which complements said essential viral gene, but is unable to cause production of new virus particles when said mutant virus infects a host cell other than said recombinant complementing host cell, for prophylactic or therapeutic use in generating an immune response in a subject infected therewith.

23. Knipe composition claim 45 reads:

A vaccine comprising a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutated herpesvirus being present in an effective immunizing amount.

24. Inglis '261 method claim 20 reads:

A method of preparing a pharmaceutical for prophylactic or therapeutic use in generating an immune response in a subject against a herpesvirus infection, said method comprising incorporating with a pharmaceutical vehicle an infectious virus, said infectious virus consisting essentially of a mutant herpesvirus which has an inactivating mutation in a viral gene, said viral gene being essential for the production of infectious new virus particles, wherein said mutant virus is able to cause production of infectious new virus particles in a recombinant complementing host cell line expressing a gene which complements said essential viral gene, but is unable to cause production of

infectious new virus particles when said mutant virus infects a host cell other than said recombinant complementing host cell.

25. Inglis '261 method claim 24 reads:

A method comprising administering to a subject a vaccine comprising a pharmaceutically acceptable excipient and an effective immunizing amount of a mutant herpesvirus, said mutant herpesvirus containing a genome in which a viral gene encoding a protein which is essential for production of infectious virus has been deleted or inactivated, wherein said mutant virus is able to cause production of infectious new virus particles in a recombinant complementing host cell expressing a gene which complements said essential viral gene, but is unable to cause production of infectious new virus particles when said mutant virus infects a host cell other than said recombinant complementing host cell, for prophylactic or therapeutic use in generating an immune response in a subject injected therewith.

26. Inglis '261 method claim 41 reads:

A method comprising administering to a subject a vaccine comprising a pharmaceutically acceptable excipient and an effective immunizing amount of an infectious virus, wherein the infectious virus in said vaccine consists essentially of a mutant herpesvirus containing a genome in which a viral gene encoding a protein which is essential for production of infectious virus has been deleted or inactivated, wherein said mutant virus is able to cause production of infectious new virus particles in recombinant complementing host cell expressing a gene which complements said

essential viral gene, but is unable to cause production of infectious new virus particles when said mutant virus infects a host cell other than said recombinant complementing host cell, for prophylactic or therapeutic use in generating an immune response in a subject infected therewith.

27. Inglis '362 method claim 13 reads:

A method of manufacturing a vaccine according to claim 1, comprising the steps of:

a) growing a mutant herpesvirus in a recombinant complementing host cell, wherein said mutant herpesvirus contains a genome in which a viral gene encoding a protein which is essential for production of infectious virus has been deleted or inactivated, and said recombinant complementing host cell expresses a gene which complements said essential viral gene: and

b) mixing the resulting virus in an effective immunizing amount with a pharmaceutically acceptable excipient.

28. Knipe method claim 12 reads:

A method of treating an immunomodulatory disease in a mammal in need thereof comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect an antibody subclass shift of IgG2a/IgG upon in vivo administration to said mammal.

29. Knipe method claim 17 reads:

A method of treating an immunomodulatory disease in a mammal in need thereof comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to effect a subclass shift of IgG2a/IgG and induce an immunological protective effect upon administration.

30. Knipe method claim 18 reads:

A method of treating an immunomodulatory disease in a mammal in need thereof comprising administering to the mammal an effective amount of a mutated herpesvirus in a pharmaceutically acceptable carrier, the herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective, said mutant herpesvirus having an ability to induce production of IFN-γ upon administration.

31. Knipe method claim 32 reads:

A method of immunizing a mammal comprising administering to said mammal a vaccine comprising a mutated herpesvirus capable of infecting a mammalian cell and of eliciting a protective response upon administration, said herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective.

32. Knipe method claim 37 reads:

A method of inducing an immune response against herpesvirus in a mammal comprising administering to said mammal a vaccine comprising a mutated herpesvirus, said herpesvirus having a mutation in one or more genes encoding a protein essential for viral replication to render the herpesvirus replication defective.

33. Knipe application 08/278,601 (the '601 application, Ex 2011) was filed on July 21, 1994 as a continuation-in-part of Knipe application 08/179,106 (the '106 application, Ex 2010). The '106 application was filed on January 10, 1994 as a continuation-in-part of Knipe application 07/922,912 (the '912 application, Ex 2009). (See Paper 68, p. 2 where Knipe admits Inglis facts 1 and 2 stated in Paper 36, p. 4).

34. The '912 application names David Knipe as the sole inventor. The later filed '106 and '601 continuation-in-part applications name David Knipe, Robert Finberg and George Sibers as co-inventors. (See Paper 68, p. 2 where Knipe admits Inglis fact 5 stated in Paper 36, p . 4).

35. Knipe has stipulated that David Knipe, Robert Finberg and George Siber are co-inventors of the invention of claims 1-8 and 12-22 of the '601 application (Paper 29, p. 2).

36. Knipe has stipulated that David Knipe is the sole inventor of the invention of claims 9, 25-27, 29 and 31-49 of the '601 application (Paper 29, p. 2).

Other findings of fact are made below.

D. Preliminary and miscellaneous motions

1. Inglis preliminary motion 8

Inglis moves pursuant to 37 CFR § 1.633(c)(4) to redefine the interfering subject matter by designating Knipe claims 31, 36 and 41 as not corresponding to the present count (Paper 40). Knipe opposes (Paper 72); Inglis replies (Paper 98).

37. Knipe admits that its claims 31, 36 and 41 recite heterologous vaccines comprising replication defective herpesviruses vectors carrying heterologous genes. (See Paper 72, p. 2 where Knipe admits Inglis facts 1-4 stated in Paper 40, p. 2).

38. Heterologous genes are genes from a foreign source. For example, if the replication defective herpesvirus is an HSV-1, then a heterologous gene can be a gene from another herpesvirus, e.g., an HSV-2, or from other infectious agents, e.g., other viruses, bacteria, fungi or parasites. A heterologous vaccine is made by inserting the heterologous gene into the herpesvirus genome. (See e.g., '601 application, Ex 2011, p. 11, l. 32 - p. 12, l. 7.)

39. A heterologous vaccine is a vaccine which induces protective immunity against pathogenic microorganisms which the vaccine does not contain. (See Cruse, p. 135).

40. Knipe's '601 application discloses that a replication defective herpesvirus mutant can be further genetically engineered to express a heterologous antigen or immunogen which elicits a protective immune response or an immunomodulation effect against the corresponding heterologous wild-type pathogen that is the source of the

heterologous gene (Ex 2011, p. 11, l. 32 - p. 12, l. 3).

41. Dr. Stephen C. Inglis has testified on behalf of Inglis (Ex 2002, ¶ 63) that:

> The vaccine carrying a heterogene might well also induce immunity against herpesvirus, but that effect would be incidental to the induction of immunity against the heterologous organism.

42. Herpesviruses are known carriers or "vectors" for delivering and regulating expression of heterologous genes (See generally Exs 2022, 1003 and 1004).

43. However, in Dr. Inglis' opinion, herpesviruses which have been mutated so as to be incapable of producing infectious progeny are not known vectors for delivering and expressing heterologous genes (Ex 2002, ¶ 64).

44. The primary examiner issued a final restriction requirement in Inglis' 08/384,963 application, from which the Inglis '362 patent issued, reasoning that claims directed to heterologous vaccines raise enablement issues not found in homologous vaccines (Ex 2021, pp. 2-3). The primary examiner stated:

> The nature of experimentation required for a chimeric [i.e., heterologous] vaccine is different from that for a non-chimeric vaccine, since protection against a heterologous pathogen involves additional issues regarding the nature of the heterologous gene chosen, expression of the heterologous gene in appropriate amounts, and expression in an appropriate location to induce the type of immune response required for protection against the heterologous pathogen. [Ex 2021, p. 2, l. 18 - p. 3, l. 1.]

Inglis' position

45. According to Inglis, Knipe claims 31, 36 and 41 define a separate patentable invention from any other claim whose designation as corresponding to the count Inglis does not dispute, i.e., Knipe claims 1-9, 12-22, 25-29, 32-35, 37-40 and 42-49; Inglis

'362 patent claims 1, 4, 5, 7, 9-13, 16, 18 and 20-24; and, Inglis '261 patent claims 1, 4, 6-8, 10-14, 16-20, 22-24, 27-28, 30 and 32-41. In other words, Inglis contends that the invention defined by Knipe claims 31, 36 and 41 are neither the same as nor obvious in view of (alone or in combination with other prior art) the invention defined by the subject matter of the nondisputed claims.

46. Further according to Inglis, Knipe claims 31, 36 and 41 are not the same as the aforementioned nondisputed claims because none of the nondisputed claims require the presence of a heterogene.

47. Still further according to Inglis, the subject matter of Knipe claims 31, 36 and 41 would not have been obvious over the subject matter of the nondisputed claims because none of the subject matter of the nondisputed claims, alone or in combination with other prior art, discloses or suggests combining a replication defective herpesvirus vector with a gene from a heterologous pathogen, or provide a reasonable expectation of success of obtaining an effective heterologous vaccine in doing so.

Discussion

The record indicates that a heterologous vaccine is designed to induce protective immunity against a pathogen which the vaccine does not contain. [See facts 38-40.]

Both Inglis and Knipe agree that herpesviruses are known carriers or "vectors" for delivering and regulating expression of heterologous genes. [See e.g., Exs 2022, 1003 and 1004.] Both Inglis and Knipe agree that a vaccine comprising a mutated herpesvirus vector carrying a heterologous gene may elicit a protective immune

response against infection by a herpesvirus. [See fact 40 and Knipe Paper 72, p. 4.]

The issue is whether the subject matter of the nondisputed claims, alone or in combination with other prior art, would have provided a reasonable expectation of success of making and using a vaccine comprising a mutated herpesvirus vector carrying a heterologous gene from pathogen X (e.g., hepatitis virus), which vaccine is capable of inducing a protective immunity against pathogen X (e.g., hepatitis virus).

Adopting the reasoning of the examiner in the restriction requirement (Ex 2021), Inglis answers "no" based on concerns which include the nature of the heterogene chosen, the amount and location of heterogene expression, and the type of immune response induced. In its reply (Paper 98, pp. 2-3), Inglis maintains that the prior art (Exs. 2022, 1003 and 1004) shows the use of herpesvirus as vectors for heterologous gene but no more.

In its opposition (Paper 72, pp. 4-5), Knipe argues that both the homologous and heterologous embodiments of the vaccine are the same patentable invention, i.e., a vaccine containing a mutated herpesvirus. Knipe further argues that it would have been obvious to one skilled in the art to use the mutated herpesvirus vaccine of the count in place of a naturally occurring herpesvirus vector for heterologous gene delivery because the mutated herpesvirus would not produce infectious progeny.

However, as pointed out by Inglis in its reply (Paper 98, p. 2), "there is no incompatibility between subgeneric status of a claim and its patentable distinctness." Moreover, Knipe's second argument does not address the issue of whether the prior art

provided a reasonable expectation of success of making and using a vaccine comprising a mutated herpesvirus vector carrying a heterologous gene from pathogen X which is capable of inducing a protective immunity against pathogen X.

Therefore, we conclude that Inglis has established that Knipe claims 31, 36 and 41 are a separate patentable invention from Count 1 (or Count 2) because the prior art fails to provide the reasonable expectation of success required to establish a prima facie case of obviousness.

Based on the foregoing, Inglis preliminary motion 8 is granted.

2. Inglis miscellaneous motion 11

Inglis moves pursuant to 37 CFR §§ 1.635 and 1.642 and Paper 25 to add pending Inglis application 08/462,632 and pending Knipe application 09/034,464 to the interference (Paper 43) contingent upon grant of Inglis preliminary motion 8.

As discussed in Inglis preliminary motion 8 above, Inglis has established that the heterologous vaccine subject matter is a separate patentable invention from the subject matter of this interference. Therefore, we decline to exercise our discretion by adding applications drawn to the heterologous vaccine subject matter, i.e., Inglis 08/462,632 and Knipe 09/034,464, to this interference.

Inglis miscellaneous motion 11 is dismissed without prejudice to further proceedings before the primary examiner as discussed infra.

3. Inglis preliminary motion 12

Inglis moves pursuant to 37 CFR § 1.633(c)(1) to redefine the interfering subject

matter by adding Inglis count 2, drawn to heterologous vaccines and uses thereof (Paper 44), to the interference, contingent upon the grant of Inglis preliminary motion 8 and Inglis miscellaneous motion 11.

First, neither Inglis patent involved in the interference, i.e., Inglis '362 and Inglis '261, have any claims drawn to heterologous vaccines and uses thereof. It is claims which give rise to an interference. If no claim of one party interferes with at least one claim of another party, then there can be no interference-in-fact.

Second, Inglis preliminary motion 11 has been dismissed without prejudice to further proceedings as discussed supra.

Third, the Knipe 09/034,464 (Knipe '464) application does not appear to have been made of record; and, Inglis has not pointed the Trial Section to where the pending Inglis application 08/462,632 (Inglis '632) and Knipe '464 claims and their status can be found in the record before us. It may be that some or all of the pending claims in Inglis '632 and/or Knipe '464 are currently rejected as unpatentable by the primary examiner in charge of the respective application.

Therefore, Inglis preliminary motion 12 is dismissed without prejudice. The possibility still exists that an additional interference may be declared to resolve the heterologous vaccine subject matter issue between pending claims in the Knipe '601, Knipe '464, and Inglis '632 applications. Inglis may wish to contact the primary examiner in charge of the Inglis '632 application to discuss the possibility of proposing an additional interference. Should the primary examiner determine that both the Knipe

and Inglis applications contain allowable claims to a heterologous vaccine, a second interference may be appropriate. 37 CFR § 1.604.

4. **Knipe miscellaneous motion 3**

Knipe moves pursuant to 37 CFR §§ 1.635 and 1.642 to add pending Inglis application 08/462,632 (the '632 application) to the interference and to designate Inglis '632 application claims 18-60 as corresponding to the count (Paper 49). Inglis opposes (Paper 81); Knipe replies (Paper 88).

For the reasons set forth in Inglis miscellaneous motion 11 and Inglis preliminary motions 8 and 12 above, we decline to exercise our discretion by adding the Inglis '632 application to the interference and designating Inglis '632 claims 18-60 as corresponding to the count.

Knipe miscellaneous motion 3 is dismissed without prejudice to Knipe seeking an additional interference (37 CFR § 1.604) drawn to the heterologous vaccine subject matter.

5. **Knipe miscellaneous motion 4**

Knipe moves pursuant to 37 CFR §§ 1.635 and 1.642 to add pending Knipe application 09/034,464 (the '464 application) to the interference and to designate Knipe '464 application claims 1-12 as corresponding to the count (Paper 50). Inglis opposes (Paper 82); Knipe replies (Paper 89).

For the reasons set forth in Inglis miscellaneous motion 11 and Inglis preliminary motions 8 and 12 above, we decline to exercise our discretion by adding Knipe

application '464 to the interference and designating Knipe claims 1-12 as corresponding to the count.

Knipe miscellaneous motion 4 is dismissed without prejudice to Knipe proceeding before the examiner and seeking an additional interference (37 CFR § 1.604) drawn to the heterologous vaccine subject matter.

6. **Knipe preliminary motion 9**

Knipe moves pursuant to 37 CFR §§ 1.633(f) and 1.633(j) to be accorded benefit for the purpose of priority of the filing date of Knipe application 07/922,912 (Paper 62), contingent upon the grant of Inglis preliminary motion 12.

Inglis preliminary motion 12 has been dismissed without prejudice as discussed supra. Therefore, Knipe preliminary motion 9 is moot. Knipe preliminary motion 9 is dismissed.

7. **Inglis miscellaneous motion 15**

According to Inglis, Inglis inadvertently failed to file a separate preliminary motion under 37 CFR § 1.633(f) for benefit of the filing dates of Inglis PCT application (Ex 2006), Inglis U.K. application 9020799.4 (the '799 application, Ex 2001), and Inglis U.K. application 9104903.1 (the '903 application, Ex 2005), contingent upon grant of Inglis preliminary motion 12.

Inglis preliminary motion 12 has been dismissed without prejudice as discussed supra. Therefore, Inglis miscellaneous motion 15 is moot. Inglis miscellaneous motion 15 is dismissed.

8. **Inglis preliminary motion 14**

Inglis moves (Paper 56) for benefit

(1) under 35 U.S.C. § 120 of the September 23, 1991 filing date of Inglis PCT application (Ex 2006),

(2) for purposes of priority of the September 25, 1990 filing date of Inglis U.K. application 9020799.4 (the '799 application, Ex 2001), and

(3) for purposes of priority of the March 8, 1991 filing date of Inglis U.K. application 9104903.1 (the '903 application, Ex 2005), contingent upon grant of Inglis preliminary motion 12. Knipe opposes (Paper 78); Inglis replies (Paper 102).

Inglis preliminary motion 12 has been dismissed without prejudice. Therefore, Inglis preliminary motion 14 is moot. Inglis preliminary motion 14 is dismissed.

9. **Inglis preliminary motion 9**

Inglis moves pursuant to 37 CFR § 1.633(c)(4) to redefine the interfering subject matter by designating Inglis U.S. Patent 5,665,362 ('362) claims 2 and 14 and Inglis U.S. Patent 5,837,261 ('261) claims 2 and 25 as not corresponding to count 1 (Paper 41). Knipe opposes (Paper 73); Inglis replies (Paper 99).

48. Inglis '362 claims 2 and 14 and Inglis '261 claims 2 and 25 further characterize the mutant herpesvirus vaccines of their respective independent claims by requiring the mutation to occur in a gene encoding a protein which is involved in a "post-replication" event (See Paper 73, p. 2 where Knipe admits Inglis facts 1 and 2 stated in Paper 41, p. 2 and Paper 99, p. 2 where Inglis admits Knipe fact 1 stated in

Paper 73, pp. 2-3).

49. Dr. Stephen C. Inglis testified on behalf of Inglis that

a) A "post-replication" event, in the context of the involved Inglis patents, refers to an event following synthesis of both new viral DNA and of new structural proteins needed for constructing progeny virus particles. [Ex 2002, ¶ 30.]

* * * * *

b) Deleting or inactivating a gene involved in a "post-replication" event, such as one encoding a essential glycoprotein, such as gH, has a number of advantages including production and release of non-infectious progeny virus particles with similar morphology (e.g., surface structures) to the normal virus and exposing the host to nearly the entire life-cycle of the virus and its associated antigens. [Ex 2002, ¶¶ 32-34.]

* * * * *

c) In contrast, the mutants described in the Knipe '912 application have mutations in the early or immediate-early genes that are required for making new viral DNA and/or causing the expression of late gene products. Thus, Knipe's mutants do not produce new progeny virus particles when they infect normal host cells because they do not produce the structural components (e.g., viral DNA and/or structural proteins, such as capsids) needed to make progeny virus particles. [Ex 2002, ¶ 29.]

50. Inglis admits that Desai (Ex 1012) discloses that the herpesvirus gH gene is essential for viral infectivity and that a herpesvirus lacking the gH glycoprotein is not infectious (See Paper 99, p. 2 where Inglis admits Knipe fact 3 stated in Paper 73, p. 3).

Inglis' position

51. According to Inglis, Inglis '362 claims 2 and 14 and Inglis '261 claims 2 and 25 define a separate patentable invention from any other claim whose designation as corresponding to the count Inglis does not dispute, i.e., Knipe claims 1-9, 12-22, 25-29, 32-35, 37-40 and 42-49; Inglis '362 patent claims 1, 4, 7, 9-13, 16, 18 and 20-24; and, Inglis '261 patent claims 1, 4, 6-8, 10-14, 16-20, 22-24, 27-28, 30 and 32-41. In other words, Inglis contends that the invention defined by Inglis '362 claims 2 and 14 and Inglis '261 claims 2 and 25 is neither the same as nor obvious in view (alone or in combination with other prior) the invention defined by the nondisputed claims.

52. Further according to Inglis, Inglis '362 claims 2 and 14 and Inglis '261 claims 2 and 25 are not the same as the aforementioned nondisputed claims because none of the nondisputed claims require a vaccine comprising a herpesvirus mutant having a mutation in a gene that encodes a protein involved in a post-replication event.

53. Still further according to Inglis, Inglis '362 claims 2 and 14 and Inglis '261 claims 2 and 25 would not have been obvious over the subject matter of the nondisputed claims because that subject matter alone, or in combination with Desai, fails to suggest the specific set of herpesvirus mutant vaccines claimed in Inglis '362 claims 2 and 14 and Inglis '261 claims 2 and 25.

Discussion

The count generically covers vaccines comprising herpesviruses that have been mutated by deleting or inactivating a gene essential for a function variously set forth as

viral replication or the production of infectious new viral particles when the vaccine mutant herpesvirus infects a normal host cell.

Inglis acknowledges that nondisputed Knipe claims 4, 8, 15, 21, 27, 35, 40 and 49 suggest vaccines comprising herpesviruses that have been mutated by deleting or inactivating the ICP8 or ICP27 gene (Paper 41, p. 4). It is part of Dr. Inglis' testimony that in "certain mutants of the ICP8 and ICP27 genes preferred by mutation according to Dr. Knipe's '912 application, a main defect could be in the control of late-gene expression, implying a defect in production of structural protein components required for making progeny virus particles" (Ex 2002, ¶ 20).

Inglis contends that the invention of Inglis '362 claims 2 and 14 and Inglis '261 claims 2 and 25 "are not broad enough to cover mutations in genes required for expression of the so-called 'late genes' or 'γ-genes'" nor in all of the late genes themselves" (Paper 41, p. 4). However, this position is viable only if the term "post-replication" event refers to event subsequent to replication of <u>both</u> the viral DNA and the viral structural proteins, as testified by Dr. Inglis (Ex 2002, ¶ 30). This definition of "post-replication" event, while plausible, is not the only definition of a "post-replicative" event in this record. According to the primary examiner, " 'replicative' refers to replication of the genome [i.e., viral DNA], and 'post-replicative' refers to events occurring between the production of progeny DNA and the production of progeny virus" in the context of the involved Inglis patents (see Ex 2019, p. 5, ¶ 2 and p. 8, ¶ 2). In other words, using the definition set forth by the primary examiner, a "post-replication"

event could cover mutations in genes required for expression of the so-called 'late genes' or 'γ-genes', such as the ICP8 and ICP27 genes required for making viral structural proteins. To the extent there is a conflict between Dr. Inglis and the primary examiner regarding the definition of a "post-replicative" event, we credit the latter over the former because we find it to be more consistent with specifications of the involved Inglis patents. For example, Inglis '362 states, "Firstly, a selected gene is inactivated within the virus genome ... This gene will be involved in the production of infectious virus, but preferably not preventing replication of the vital [sic, viral] genome" (Ex 2003, c. 3, ll. 5-9) (see also Inglis '261, Ex 2004, c. 2, ll. 44-49 and c. 3, ll. 18-20). Further, Inglis has not pointed to where either Inglis '362 or Inglis '261 supports the exclusive definition of "post-replicative" event urged by Dr. Inglis in his testimony. Therefore, we find that Inglis has not established that Inglis '362 claims 2 and 14 and Inglis '261 claims 2 and 25 define a separate patentable invention as the invention of nondisputed Knipe claims requiring a vaccine comprising a herpesvirus that have been mutated by deleting or inactivating the ICP8 or ICP27 gene.

In its opposition (Paper 73, p. 4), Knipe argues that it would have been obvious within the meaning of 35 U.S.C. § 103 to use a herpesvirus mutated with respect to the gH glycoprotein in the vaccine of the count because Desai (Ex 1012) discloses that a herpesvirus lacking the gH glycoprotein is not infectious.

To establish a prima facie case of obviousness, there must be both some suggestion or motivation to modify the reference or combine reference teachings and a

reasonable expectation of success. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991). Knipe has pointed out a specific motivation to use a herpesvirus with a specific mutation involving the gene encoding the gH glycoprotein, i.e., a herpesvirus lacking the gH glycoprotein is not infectious.

Inglis replies (Paper 99, p. 3) that Desai is concerned with studying the function of the gH glycoprotein and is silent as to vaccines. Desai is not limited to what it expressly teaches, but what inferences one of ordinary skill in the vaccine art reasonably would draw from it. In re Lamberti, 545 F.2d 747, 750, 192 USPQ 278, 280 (CCPA 1976).

Therefore, we conclude that Inglis has not established that Inglis '362 claims 2 and 14 and Inglis '261 claims 2 and 25 are a separate patentable invention from the nondisputed claims of the count.

Based on the foregoing, Inglis preliminary motion 9 is denied.

10. Inglis preliminary motion 10

Inglis moves pursuant to 37 CFR § 1.633(c)(4) to redefine the interfering subject matter by designating Inglis '362 claims 3, 6, 8, 15, 17 and 19 and Inglis '261 claims 3, 5, 9, 15, 21, 26, 29 and 31 as not corresponding to count 1 (Paper 42). Knipe opposes (Paper 74); Inglis replies (Paper 100).

54. The claims subject to this motion characterize the mutant herpesvirus vaccines of the count as

a) deleting or inactivating a gene encoding an essential protein not required for

virus assembly, but necessary for the assembled virus to be able to infect new cells (Inglis '362 claims 3 and 15; Inglis '261 claims 3 and 26);

b) deleting or inactivating a gene encoding a glycoprotein (Inglis '362 claims 6 and 17; Inglis '261 claims 9, 21 and 29);

c) deleting or inactivating a gene encoding glycoprotein gH (Inglis '361 claims 8 and 19; Inglis '261 claims 15 and 31); and

d) allowing production and release of non-infectious viral particles from normal host cells (Inglis '261 claim 5).

(See Paper 74, p. 2 where Knipe admits Inglis facts 2-5 stated in Paper 42, pp. 2-3).

55. A vaccine comprising a herpesvirus containing a deleted or inactivated gH gene is an example of the type of mutation recited in the claims subject to this motion (see Paper 74, p. 2 where Knipe admits Inglis fact 7 stated in Paper 42, p. 3).

Inglis' position

56. According to Inglis, Inglis '362 claims 3, 6, 8, 15, 17 and 19 and Inglis '261 claims 3, 5, 9, 15, 21, 26, 29 and 31 define a separate patentable invention from any other claim whose designation as corresponding to the count Inglis does not dispute, i.e., Knipe claims 1-9, 12-22, 25-29, 32-35, 37-40 and 42-49; Inglis '362 patent claims 1, 4, 7, 9-13, 16, 18 and 20-24; and, Inglis '261 patent claims 1, 4, 6-8, 10-14, 16-20, 22-24, 27-28, 30 and 32-41. In other words, Inglis contends that the invention defined by Inglis '362 claims 3, 6, 8, 15, 17 and 19 and Inglis '261 claims 3, 5, 9, 15, 21, 26, 29 and 31 is both novel and unobvious over the invention defined by the nondisputed

claims.

57. Further according to Inglis, none of the nondisputed claims require inactivating or deleting a gene that (a) encodes an essential protein not required for virus assembly, but necessary for the assembled virus to be able to infect new host cells, (b) a glycoprotein, (c) glycoprotein gH or (d) allows production and release of non-infectious viral particles from infected normal host cells.

58. Still further according to Inglis, the subject matter of Inglis '362 claims 3, 6, 8, 15, 17 and 19 and Inglis '261 claims 3, 5, 9, 15, 21, 26, 29 and 31 would not have been obvious over the subject matter of the nondisputed claims because there is no suggestion of the specifically claimed mutants.

Discussion

The count generically covers vaccines comprising herpesviruses that have been mutated by deleting or inactivating a gene essential for a function variously set forth as viral replication or the production of infectious new viral particles when the vaccine mutant herpesvirus infects a normal host cell.

A vaccine comprising a herpesvirus containing a deleted or inactivated gH gene is an example of the type of mutation recited in the claims subject to this motion. In its opposition (Paper 74, p. 5), Knipe argues that it would have been obvious within the meaning of 35 U.S.C. § 103 to use a herpesvirus mutated with respect to the gH glycoprotein gene in the vaccine of the count because Desai (Ex 1012) discloses that a herpesvirus lacking the gH glycoprotein is not infectious.

Contrary to Inglis' contention that a herpesvirus mutated with respect to the gH glycoprotein gene would only be obvious given a hindsight reading of Inglis' disclosure (Paper 100, p. 2), we find that Knipe has established the existence of sufficient motivation for selecting a herpesvirus mutated with respect to the gH glycoprotein gene, i.e., the mutant is not infectious (Paper 74, p. 5).

Therefore, for the above reasons and reasons set forth in our discussion of Inglis preliminary motion 9, we find that Inglis has failed to establish that Inglis '362 claims 3, 6, 8, 15, 17 and 19 and Inglis '261 claims 3, 5, 9, 15, 21, 26, 29 and 31 define a separate patentable invention from any other claim whose designation as corresponding to the count Inglis does not dispute.

Based on the foregoing, Inglis preliminary motion 10 is denied.

11. **Knipe preliminary motion 5**

Knipe preliminary motion 5 (Paper 51) seeks entry of amendments to claims 25 and 42 and addition of new claims 50-54 under 37 CFR § 1.633(c)(2) and § 1.633(i). Knipe preliminary motion 5 was filed in response to Inglis preliminary motions 4, 5 and 6 under 37 CFR § 1.633(a). Inglis opposes (Paper 83); Knipe replies (Paper 90).

Knipe's position

59. According to Knipe, claims 25 and 42, as amended, and added claims 50-54 are directed to the same patentable invention as claims which have been designated as corresponding to (a) the present count and (b) the proposed count in Knipe preliminary motion 1 (Paper 47).

60. Further according to Knipe, the subject matter of the amended and added claims is described in the '061 application (Ex 2011) as follows:

amended claim 25 from p. 2, l. 27 to p. 3, l. 8, and in the examples,

amended claim 42 from p. 2, l. 27 to p. 3, l. 8, and in the examples,

added claims 50-53 from p. 2, l. 27 to p. 3, l.8, and in the examples, and

added claim 54 from p. 2, l. 27 to p. 3, l. 8, and in the examples.

61. The "Summary of the Invention" section of the Knipe application '601 reads in part from p. 2, l. 27 to p. 3, l. 8:

> The invention features a herpesvirus vaccine comprising a mutated herpesvirus in a pharmaceutically acceptable carrier. The mutated herpesvirus is capable of infecting cells of the mammal to be vaccinated, and it is capable of eliciting a protective immune response in that mammal and/or inducing an immunomodulatory response as evidenced by an antibody subclass shift when administered in vivo to that mammal. The mutation occurs in at least one gene encoding a protein essential for replication of the virus, so that the mutation renders the virus replication defective. The mutated virus is live in the sense that it retains the ability to infect target cells in the host to be protected. Infection will not produce progeny, yet the virus elicits a protective immune response, e.g., via virally induced or encoded immunogens produced by infected cells.

62. Knipe maintains that it is not aware of any prior art which describes or renders obvious the claimed subject matter to one of ordinary skill in the art.

63. According to Knipe, the requirements of 37 CFR §§ 1.633 and 1.637 have been met.

Discussion

Knipe must comply with 37 CFR § 1.637(c)(2) in addition to complying with the other requirements of a 37 CFR § 1.633(c) motion.

According to 37 C.F.R § 1.637(c)(2)(iii), the movant must show the "patentability" to the applicant of each claim proposed to be amended or added.

A notice of the Chief Administrative Patent Judge addresses the issue of how one should interpret rules that require a Party to "show the patentability" of a claim in 1217 Off. Gaz. Pat. & Tm. Office 17-18 (December 1, 1998). The notice explains:

> The requirement of the rules that a party "show the patentability" of a claim may have led to some confusion as to precisely what is required to comply with the rules. This notice provide guidance with respect to the requirement to "show the patentability."
>
> The requirement that a party "show the patentability" of a claim should not be construed as requiring a party to prove a negative, i.e., that there is no prior art which would anticipate the claim under 35 U.S.C. § 102 or render the claims unpatentable under 35 U.S.C. § 103. In this respect, the burden of establishing that claim is not patentable generally falls on the party or individual alleging unpatentability. See e.g., 35 U.S.C. §102 which provides that an applicant is "entitled to a patent unless ***." See also, Horton v. Stevens, 7 USPQ2d 1245, 1246-47 (Bd. Pat. App. & Int 1988). Consistent with 37 CFR § 1.601, which provides that the rules should be construed to secure the just, speedy and inexpensive determination of interferences, the rules requiring a party to "show the patentability" of a claim normally should be interpreted as requiring that a party establish that the subject matter of the claim is described in the specification in the manner required by the first paragraph of 35 U.S.C. § 112. See also 37 CFR § 1.75(d)(1). The requirement can most effectively be met by reproducing the claim, and following each element recited in the claim, and within braces {} and in bold, insert a specific reference to the column and line and/or drawing figure and numeral where the element is described in the specification.
>
> An exception would be a situation where a party files a preliminary motion under 37 CFR § 1.633(i) in response to an opponent's preliminary motion under 37 CFR § 1.633(a) for judgment. Since the party knows the basis for the opponent's preliminary motion for judgment, the party should also "show the patentability" of the claims proposed to be added by the preliminary motion under 37 CFR § 1.633(i) vis-a-vis the opponent's basis in the preliminary motion under 37 CFR § 1.633(a). Compare 37 CFR §§

1.111(c) and 1.119 [(1998)].

The precise basis upon which a party is required to "show the patentability" necessarily will vary on a case-by-case basis.

Knipe has not met the requirements of 37 C.F.R § 1.637(c)(2)(iii).

64. The specification of Knipe application '601 (Ex 2011) is sixty-one pages long.

65. The examples begin on p. 16 and end on p. 61 of the '601 specification (Ex 2011).

It is not the role of the Trial Section to review a partial "Summary of the Invention" and shift through over forty-five pages of examples in a specification to determine or establish whether or not the subject matter of the amended and added claims is described in the specification in the manner required by the first paragraph of 35 U.S.C. § 112.

Knipe has not correlated each element recited in each amended and added claim with specific reference to column and line and/or drawing figure and numeral in application '601 to show where the element is described. See also paragraph 21 of the NOTICE DECLARING INTERFERENCE (Paper 1) which requires specifying reference to page and line of specification and/or figure and item number of drawing within braces when a new claim is presented.

Furthermore, according to 37 CFR § 1.637(c)(2)(ii), the movant must show that the claim proposed to be amended or added defines the same patentable invention as the count. As stated in 37 CFR § 1.601(n), invention "A" is the same patentable

invention as invention "B" when invention "A" is the same as (35 U.S.C. §102) or is obvious (35 U.S.C. §103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A."

According to Knipe (Paper 51, p. 4), amended claims 25 and 42 and added claims 50-54 "are directed" to the same invention as claims which have been designated as "corresponding" to the present count and the proposed count advanced in Knipe preliminary motion 1 (Paper 47). While the count is defined by multiple claims in the alternative, all of the claims designated as "corresponding" to the count are not part of the count. Knipe has not shown that amended claims 25 and 42 and added claims 50-54 are anticipated by or obvious over any claims which define the count.

Therefore, entry of the proposed amended and added claims is denied for non-compliance with the requirements of Rule ~~187~~ 637(c)(2)(ii) and (iii) and paragraph 21 of the NOTICE DECLARING INTERFERENCE.

12. Knipe preliminary motion 1

Knipe moves pursuant to 37 CFR § 1.633(c) to substitute Knipe "proposed count 1" for count 1 contending that Knipe claims 1-8 and 12-22 define a separate patentable invention from Knipe claims 9, 25-27, 29 and 31-49 (Paper 47). Knipe "proposed count 1" is (material deleted from present count 1 shown in strikeout):

A composition according to Claim 1 of Inglis '261 or any of Claims 1 or 24 of Inglis '362 or any of Claims ~~1, 5,~~ 9, 25, or 42-45 of Knipe

or

a method according to any of Claims 20, 24, or 41 of Inglis '261 or Claim 13 of Inglis '362, or any of Claims ~~12, 17, 18,~~ 32 or 37 of Knipe.

As a result of our decision on Inglis preliminary motions 4 through 7 infra and Inglis preliminary motion 8 supra, the interference will be redeclared by substituting Count 2 for the present Count 1 in a separate paper accompanying this MEMORANDUM ORDER AND OPINION. Count 2 will be:

A composition according to claim 1 of Inglis '261 or any of claims 1 or 24 of Inglis '364 or a method according to any of claims 20, 24 or 41 of Inglis '261 or claim 13 of Inglis '362.

The claims of the parties are:

Inglis '261:	1-41
Inglis '362:	1-24
Knipe:	1-9, 12-22, 25-27, 29, 31-49

The claims of the parties which correspond to Count 2 are:

Inglis '261:	1-41
Inglis '362:	1-24
Knipe:	1-9, 25-27, 29, 32-35, 37-40 and 42-49

The claims of the parties which do not correspond to Count 2, and therefore are not involved in the interference on the issue of priority, are:

Inglis '261:	None
Inglis '362:	None

Knipe: 12-22, 31, 36 and 41

In effect, Count 2 provides Knipe with the relief sought insofar as it omits Knipe claims 1, 5, 12, 17 and 18 from Count 2.[8] However, the following comments are made for completeness.

Knipe claims 31, 36 and 41 recite heterologous vaccine subject matter which is patentably distinct from the subject matter of Count 2 for reasons given supra in our decision on Inglis preliminary motion 8. As to Knipe claims 1-8, Knipe (Paper 87, p. 2) does not dispute Inglis' argument (Paper 79, pp. 5-6, 9 and 11) that Knipe composition claims 1-8 correspond to the subject matter of Knipe's "proposed count 1" because recitation of inherent features of a composition does make that composition patentable.[9] In re Papesch, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963) is often cited for its statement that "a chemical compound and all of its properties are inseparable." However, as to Knipe claims 12-22, methods of using a composition based upon its unknown specific property, i.e., the ability to effect an antibody subclass shift of IgG2a/IgG (claims 12-17) and/or to induce production of IFN-γ (claims 17-22) upon in vivo administration to a mammal, would not have been obvious unless that composition were already known in the prior art to be useful for that same purpose. Knipe states (a) that it is unaware of any prior art which describes or suggests that a composition comprising a mutant herpesvirus capable of effecting an antibody subclass

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[8] See our decision on Inglis preliminary motion 4 infra where Knipe claims 1 and 5 are held to be unpatentable.

[9] Inglis' arguments also apply to Count 2.

shift of IgG2a/IgG or inducing production of IFN-γ is useful for treating immunomodulatory disease and (b) that such use would not have been obvious from the use of a mutant herpesvirus as a herpes vaccine. Inglis has not submitted meaningfully evidence or argument to rebut Knipe's position.

Therefore, Knipe preliminary motion 1 is granted only to the extent that Knipe claims 12-22 will be designated as not corresponding to Count 2; it is otherwise denied.

Further since Knipe claims 12-15, 17-21, 36 and 41 are no longer involved in the interference defined by Count 2, to the extent our decision on Inglis preliminary motions 6 and 7 infra addresses the patentability of Knipe claims 12-15, 17-21, 36 and 41 it is a recommendation under 37 CFR § 1.659(a).[10]

13. Knipe preliminary motion 2

Knipe moves pursuant to 37 CFR § 1.633(f) for benefit for the purpose of priority of the July 21, 1992 filing date of Knipe's application 07/922,912 (the '912 application, Ex 2009) (Paper 48) contingent upon grant of Knipe preliminary motion 1. Knipe preliminary motion 2 is moot in view of redeclaring the interference by substituting Count 2 for the present Count 1. Therefore, Knipe preliminary motion 2 is dismissed.

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[10] According to 37 CFR § 1.659(a),

> Should the Board have knowledge of any ground for rejecting any application claim not involved in the judgment of the interference, it may include in its decision a recommended rejection of the claim. Upon resumption of ex parte prosecution of the application, the examiner shall be bound by the recommendation and shall enter and maintain the recommended rejection of unless an amendment or showing of facts not previously of record is filed which, in the opinion of the examiner, overcomes the recommended rejection.

14. Inglis preliminary motion 13

Inglis moves pursuant to 37 CFR § 1.683(j) [sic, 1.633(f)] for benefit for the purpose of priority of the filing dates of Inglis' PCT application (Ex 2006), UK application '799 (Ex 2001) and UK application '903 (Ex 2005) (Paper 54) contingent upon grant of Knipe preliminary motion 1. Inglis preliminary motion 13 is moot in view of redeclaring the interference by substituting Count 2 for the present Count 1. Therefore, Inglis preliminary motion is dismissed.

15. Knipe preliminary motion 6

Knipe moves pursuant to 37 CFR §§ 1.633(c)(1) and 1.633(i) to substitute Knipe "revised proposed count 1" for count 1, contending that Knipe claims 1-8 and 12-22 define a separate patentable invention from Knipe claims 9, 25-27, 29 and 31-49; and, to add amended claims 25 and 42 and added claims 50-54 as claims which in the alternative define the count (Paper 58). Knipe "revised proposed count 1" is identical to Knipe "proposed count 1," except that Knipe "revised proposed count 1" would include Knipe claims 25 and 42 as amended and further include new claims 50-54.

First, for the reasons discussed in Knipe preliminary motion 1 supra, we are redeclaring the interference by substituting Count 2 for Count 1. Second, Count 2 provides Knipe with part of the relief sought insofar as it omits Knipe claims 1, 5, 12, 17 and 18 from Count 2. Third, the remainder of the relief sought by Knipe is moot since entry of amended claims 25 and 42 and added claims 50-54 has been denied for noncompliance with 37 CFR §§ 1.637(c)(2)(ii) and 1.637(c)(2)(iii) and paragraph 21 of

the NOTICE DECLARING INTERFERENCE. Therefore, Knipe preliminary motion 6 is dismissed.

16. **Knipe preliminary motion 7**

Knipe moves pursuant to 37 CFR § 1.633(f) for benefit for priority purposes of the July 21, 1992 filing date of Knipe's application 07/922,912 (the '912 application, Ex 2009) (Paper 59) contingent upon grant of Knipe preliminary motion 6. Knipe preliminary motion 7 is moot because Knipe preliminary motion 6 has been dismissed. Therefore, Knipe preliminary motion 7 is dismissed.

17. **Inglis preliminary motion 7**

Inglis preliminary motion 7 (Paper 39) seeks entry of judgment as to Knipe claims 12-15 and 17-21 under 37 CFR § 1.633(a). According to Inglis, Knipe claims 12-15 and 17-21 do not comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. Knipe has opposed (Paper 71); Inglis has replied (Paper 97).

We dismiss the motion since Knipe claims 12-15 and 17-21 have been designated as not corresponding to Count 2 and therefore are no longer involved in this interference. However, based upon the findings and analysis below, we exercise our discretion under 37 CFR § 1.659(a) and enter a recommendation that Knipe claims 12-15 and 17-21 be rejected under 35 U.S.C. § 112, first paragraph.

66. Knipe claims 12-15 and 17-21 are directed to methods of treating an immunomodulatory disease in a mammal by administration of an effective amount of a replication defective herpesvirus mutant to the mammal. The herpesvirus mutant is

able to induce an antibody IgG2a/IgG subclass shift upon in vivo administration (Knipe claims 12-15 and 17) and/or induce production of IFN-γ upon administration (Knipe claims 17-21).

67. Knipe application 08/278,601 (the '601 application) is Ex 2011.

68. Knipe describes the invention as follows (Ex 2011):

a) This invention relates to a method of treating an immunopathologic, immunomodulatory or immunoregulatory disease or condition, e.g., herpetic stromal keratitis or encephalitis, by inducing an immunomodulatory response as evidenced by an antibody subclass shift [p. 4, ll. 4-10 and p. 14, ll. 26-32].

* * * * *

b) The mutated herpesvirus is capable of infecting cells of the mammal to be vaccinated and of eliciting a protective immune response in that mammal and/or inducing an immunomodulatory response as evidenced by an antibody subclass shift when administered in vivo to that mammal [p.2, ll. 29-34].

* * * * *

c) The vaccine should induce both protective humoral antibodies and cell-mediated immunity [p. 10, ll. 33-35].

* * * * *

d) The effect can be viewed as a virus-induced immunomodulation [p. 13, ll. 18-19].

69. Immunomodulation is a therapeutic alteration of the immune system by the

administration of biological response modifiers such as lymphokines and antibodies (See Cruse, p. 162).

70. Immunopathology is the study of disease processes that have an immunological etiology or pathogenesis involving either humoral antibody (from B cells) and complement or T cell-mediated mechanisms. Id.

71. Knipe reveals that (Ex 2011):

a) Psolaren-inactivated virus and immediate-early infected cell protein 4 (ICP4) mutant virus d120 failed to induce the antibody subclass shift in mice [p. 50, l. 25 - p. 51, l. 9].

* * * * *

b) Two replication-defective mutant viruses with late replication blocks, i.e., ICP27 mutant virus n504 and ICP8 mutant virus d301, induced the antibody subclass shift in mice [p. 51, ll. 10-31].

72. Switching to mouse IgG2a isotype responses is induced by IFNγ and suppressed by IL-4. Little is known about the control of human IgG subclass expression. Switching to IgG isotypes may be controlled very differently in mice than in humans. (See Fields, p. 842, "Mouse IgG2a" and p. 842, "Human IgG.")

Inglis' position

73. Inglis maintains that Knipe claims 12-15 and 17-21 fail to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph.

74. According to Inglis, Knipe application '601 does not enable one of ordinary

skill in the art to treat the genus of "immunomodulatory diseases" without undue experimentation, citing In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

75. Further according to Inglis, the term "immunomodulatory disease" is not a term of art and has not been defined by Knipe. Inglis reasons that giving the term its broadest reasonable interpretation, "immunomodulatory disease" covers any disease condition, regardless of causative agent, that modulates the immune system. See Testimony of Stephen C. Inglis (Ex 2002, para. 60). Thus, Inglis concludes that Knipe claims 12-15 and 17-21 can be construed as covering methods of treating nearly all diseases in mammals.

76. Inglis does not challenge Knipe method claims 16 and 22 which are limited to treating a specific disease condition, i.e., herpetic stromal keratitis.

Discussion

The enablement clause 35 U.S.C. § 112, first paragraph, requires that the patent specification enable "those skilled in the art to make and use the full scope of the claimed invention without 'undue experimentation.'" Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether making or using the invention would have required undue experimentation, and thus whether the disclosure is enabling, is a question of law to be resolved based upon several underlying factual inquiries. See Wands, 858 F.2d, 731, 735, 736-37, 8 USPQ2d, 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in Wands, the factors which

may be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. It was held in In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970), that in cases which involve unpredictable factors such as physiological activity, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved."

Based on our reading of Knipe application '601 (Ex 2011), "immunomodulatory disease" broadly encompasses any disease in any mammal, human or nonhuman, involving a change in either antibody production and/or cell-mediated immune response of the immune system of the mammal to any immunological agent, e.g., bacteria, DNA and viruses.

In its opposition (Paper 71, p. 4), Knipe argues that enablement does not require the '601 application to show that the method of claims 12-15 and 17-21 is effective for treating "all" immunomodulatory diseases. Inglis agrees that Knipe does not need to disclose effectiveness in the treatment of "all" immunomodulatory diseases (Paper 97, p. 4). However, "the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art." Id., at 839, 166 USPQ at 24. See also PPG Industries Inc. v Guardian Industries

Corp., 75 F.3d 1558, 1564, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996) ("In unpredictable art areas, this court has refused to find broad generic claims enabled by specifications that demonstrate the enablement of only one or a few embodiments and do not demonstrate with reasonable specificity how to make and use other potential embodiments across the full scope of the claim.").

Although Inglis is incorrect in stating that the Knipe '601 application only discloses one example of such an immunomodulatory disease, i.e., herpetic stromal keratitis (Paper 39, p. 2 and Paper 97, p.3), the Knipe '601 application only describes a single immunomodulatory disease type, i.e., herpetic disease. Herpetic disease is caused by a single immunological agent, i.e., herpes virus. (The '601 application describes both herpetic stromal keratitis and encephalitis (Ex 2011, p. 14, ll. 26-32)). Thus, Wands factors (2) and (8) support a conclusion of lack of enablement.

According to Knipe, herpesvirus induced immunomodulation is evidenced by occurrence of an antibody subclass shift in a mammal upon administration of a vaccine consisting essentially of replication defective herpesvirus mutant to that mammal. However, there is evidence that some replication defective herpesvirus mutants, e.g., d301 and n504, but not others, e.g., d120, have the ability to induce an antibody subclass shift. Moreover, mice were the only mammals tested to obtain the data presented in the '601 application (see e.g., Ex 2011, pp. 50-52). Since little is known in the prior art about the control of human IgG subclass expression (see Fact 44 supra), the data obtained using mice may or may not be capable of extrapolation to another

mammal, such as a human. Moreover, an immune response is a physiological activity. Based on these facts, Wands factors (2), (3), (5), (7) and (8) support a conclusion of lack of enablement.

Based on our reading of the record, at least five Wands factors support a conclusion of lack of enablement. These factors are (8) the breadth of the claims, (2) and (3) the limited disclosure in the application, (5) the state of the prior art as to human IgG subclass regulation and (7) the unpredictability shown by the fact that only some replication defective herpesvirus mutants induced the IgG2a/IgG subclass shift and the physiological nature of an immune response. Accordingly, we conclude Inglis has established that the '601 specification does not enable those skilled in the art to make and use the invention of claims 12-15 and 17-21 throughout its scope without undue experimentation.

In its opposition (Paper 71, p. 4), Knipe argues that the Patent Office has made a clear statement that Knipe claims 12-15 and 17-21 comply with the requirements of 35 U.S.C. § 112 by virtue of declaring this interference and designating Knipe claims 12-15 and 17-21 among those corresponding to the count. Knipe's argument is apparently based on an ex parte decision of the primary examiner forwarding papers to the Board for declaration of interference. A preliminary motion based on a lack of enablement is not an appeal from a decision of an examiner. Cf. Glaxo Wellcome, Inc. v. Cabilly, 56 USPQ2d 1983 (Bd. Pat. App. & Int. 2000) (binding Trial Section precedent). In any event, arguments presented by Inglis in this interference have not

been shown by Knipe to have been considered by the primary examiner. Independent of any decision by the primary examiner, we find the Inglis arguments to be persuasive.

Based on the record before us, a preponderance of the evidence supports a conclusion that one skilled in the art would not be enabled to make and use the invention of claims 12-15 and 17-21 without undue experimentation.

Inglis preliminary motion 7 is dismissed and we recommend Knipe claims 12-15 and 17-21 be rejected for failure to comply with the enablement requirement of 35 U.S. C. § 112, first paragraph. 37 CFR § 1.659(a).

18. Inglis preliminary motion 4

Inglis preliminary motion 4 (Paper 36) seeks entry of judgment as to Knipe claims 1-8, 25-27 and 29 under 37 CFR § 1.633(a). According to Inglis, Knipe claims 1-8, 25-27 and 29 are unpatentable under 35 U.S.C. § 102(b) over Nguyen (Ex 2012) and under 35 U.S.C. § 102(f) over Knipe application 07/922,912 (Ex 2009).

77. Inglis has provided an element-by-element comparison between Knipe claims 1-8, 25-27 and 29 and the disclosure of Nguyen (Claim chart, Ex 2014).

78. Inglis has provided an element-by-element comparison between Knipe claims 1-8, 25-27 and 29 and the disclosure of Knipe's application 07/922,912 (Claim chart, Ex 2013).

Discussion

Inglis preliminary motion 4, when considered in light of the evidence relied upon in support of the motion, establishes a sufficient basis for holding Knipe claims 1-8, 25-

27 and 29 to be unpatentable under 35 U.S.C. § 102(b) over Nguyen.

Knipe does not oppose Inglis preliminary motion 4 with respect to claims 1-8 (Paper 68, p. 2). Knipe has not submitted any meaningful evidence in opposition to Inglis preliminary motion to defend the patentability of unamended claims 25-27 and 29 (See Paper 68).

In its opposition (Paper 68, pp. 3-4), Knipe argued that the July 24, 2000 amendment (Ex 1005) obviated the "rejections" of claims 25-27 and 29. However, that amendment (Ex 1005) was denied entry when Knipe preliminary motion 5 was denied.

Accordingly, Inglis preliminary motion 4 urging unpatentability under § 102(b) with respect to Knipe claims 1-8, 25-27 and 29 is granted. Because we grant the motion with respect to § 102(b), we have not found it necessary to consider or decide Inglis preliminary motion 4 to the extent it is based on §102(f).

19. Inglis preliminary motion 5

Inglis preliminary motion 5 (Paper 37) seeks entry of judgment under 37 CFR § 1.633(a) as to Knipe claims 42, 45, 47 and 48. According to Inglis, Knipe claims 42, 45, 47 and 48 are unpatentable to Knipe under 35 U.S.C. § 102(b) over either Inglis PCT application (WO 92/05263, Ex 2006) or Nguyen (Ex 2012). Knipe opposes (Paper 69); Inglis replies (Paper 95).

79. Inglis has provided an element-by-element comparison between Knipe claims 9, 32-34, 37-39 and 42-48 and the disclosures in both the Inglis PCT application and in Nguyen (Claim chart, Ex 2015).

Knipe seems to concede that the Inglis PCT application and Nguyen anticipate claims 42, 45, 47 and 48 under 35 U.S.C. § 102(b) if the claims are not accorded benefit of the July 31, 1992 filing date of the '912 grandparent application (Paper 69). Accordingly, the dispositive issue is whether claims 42, 45, 47 and 48 are entitled to benefit under 35 U.S.C. § 120 of the July 31, 1992 filing date of the '912 application.

80. Knipe admits that claims 42-48 were added to the '601 application on September 8, 1998, after the '601 application was filed. Knipe admits that claim 42 was modeled on Inglis '362 for purposes of provoking an interference. [See Paper 69, p. 2 where Knipe admits Inglis Fact 3 stated in Paper 37, p. 3.]

81. The '912 application (Ex 2009) discloses:

> The invention features a herpesvirus vaccine comprising a mutated herpesvirus suspended in a pharmaceutically acceptable carrier. The mutated herpesvirus is capable of infecting cells of the mammal to be vaccinated, and it is capable of eliciting a protective immune response in that mammal. The mutation occurs in at least one gene encoding a protein essential for replication of the virus, so that the mutation renders the virus replication defective. Specifically, the virus is live in the sense that it generally retains the ability to infect target cells in the host to be protected. Infection will not produce progeny, yet the virus elicits a protective immune response, e.g., via virally induced or encoded immunogens produced by infected cells. [P. 2, ll. 20-33.]
>
> * * * * *
>
> Specifically, vaccine candidates according to the invention should have at least the following properties: they should be viable and yet be effectively incapable of producing viable progeny virus in the host into which they are introduced; and they should be capable of inducing a protective immune response in that host. Any viable herpesvirus which is incapable of replication (in the absence of an exogenous source of the protein, such as from a supporting host cell line expressing complementing genes) and is therefore incapable of generating progeny virus, but which is capable of expression of antigenic determinants such that a protective immune response is induced, is a potential vaccine

candidate. [P. 11, ll. 11-23.]

82. The '912 application (Ex 2009) further discloses:

a) Candidate viruses for the vaccine can be screened for the appropriate mutation by selecting viruses able to replicate only in the presence of an exogenous source of the essential protein, e.g., a cell line expressing complementing genes [p. 10, ll. 24-28].

* * * * *

b) Candidate viruses for the vaccine may contain mutations in the ICP27 or ICP8 genes or in genes encoding capsid proteins. Glycoprotein immunogens, such as gB, gD and gH, may be inserted into a mutated background. [P. 15, ll. 16-29.]

83. Dr. Stephen C. Inglis testified on behalf of Inglis that (Ex 2002, ¶ 23):

> Dr Knipe's '912 application as a whole supports the understanding that the 'replication defective' viruses of the Knipe '912 application are viruses producing no progeny when they infect normal cells. The '912 application indicates in several places that the "replication defective" viruses produce no progeny. See, for example page 2, lines 30-31, which states in the overall summary of the invention that "Infection will not produce progeny." This is repeated elsewhere, e.g., at page 11 line 20: "Incapable of generating progeny virus". Progeny is understood as meaning progeny virus particles. The '912 application conveys that the mutant viruses do not replicate to produce virus particles when they infect a normal host cell (although they can produce virus particles when cultured on complementing cell lines).

84. Dr. Edward S. Mocarski, Jr. testified on behalf of Inglis that (Ex 2024, ¶¶ 5-6 and 29):

> Application 07/922,912 concerns the vaccine uses of certain mutant herpesviruses, carrying a mutation disabling an essential replication gene. From the application as a whole, one skilled in the art would understand

> that such a mutant has to be replication-defective. The expression 'replication defective' has some ambiguity and would be understood according to its context. In context here, one skilled in the art would understand that such a mutation has to block production of progeny virus particles when the mutant virus infects a normal host cell in culture or in a vaccine. [Ex 2024, ¶ 5.]
>
> The preference set forth in the application is to choose ICP8 and/or ICP27 genes for mutation. I have also considered the paragraph on page 15 at lines 16-21, containing reference to 'any viral mutant which ... is replication defective', and to 'viruses containing mutations in genes encoding capsid proteins'. One skilled in the art would understand these particular proposals in context, and that they are consistent with the remainder of the teaching. It would be understood that they propose replication-defective mutants from which there is no production of progeny virus particles when the mutant virus infects a normal host cell or a cell of a vaccinee. [Ex 2024, ¶ 6.]
>
> Accordingly, the mutants described in the '912 application are mutants with defects in the (early or immediate-early) genes that are required for making new virus genomes and/or for causing expression of viral late gene products, and they are mutants that produce no new viral particles when they infect normal cells.
>
> For the above reasons the '912 application clearly uses the words 'replication defective' to mean that the mutant virus either fails to make the new viral DNA needed for constructing progeny virus particles, or it fails to make the new structural proteins required for constructing progeny virus particles, or both. [Ex 2024, ¶ 29.]

85. Dr. Edward S. Mocarski, Jr. later testified on behalf of Inglis (Ex 2035, ¶ 7) in reply to testimony of Dr. Neal DeLuca (Ex 1009):

> In reply, I confirm that I have read Dr. Knipe's '922 [sic] patent application as it would be read by a person skilled in the art. That is, the '922 [sic] application identifies clearly on page 2 lines 30-31 and elsewhere that the mutants produce no progeny. The '922 [sic] application nowhere suggests using mutants that produce non-infectious progeny. The only viral genes that '922 [sic] points out and recommends for mutation are (early) genes that it states (page 1-2) to be required for viral DNA replication and/or for the expression of late viral genes. Accordingly I

believe that the reading of the '922 [sic] specification offered by Dr. Inglis, which as criticized as "biased" by Dr DeLuca in his paragraph 24, is in fact in agreement with my own views as to what the '912 application conveys to a person skilled in the art. This reading does not appear to me to be biased.

86. Dr. Neal DeLuca testified on behalf of Knipe (Ex 1009), referring to the "Knipe Application" 09/022,912 (Ex 1009, ¶ 2), that

> In my opinion, one of ordinary skill in the art in reading the Knipe Application would have understood that Dr. Knipe was in possession of an invention that is directed to a vaccine that is comprised of a mutated herpes virus wherein the mutation prevents the production of infectious viral progeny. [Ex 1009, ¶ 4.]
>
> In fact, the inventor unequivocally states that a mutated herpes virus in accordance with the invention is "effectively incapable of producing viable progeny virus in the host....", which statement indicates to one of ordinary skill in the art that the mutated virus does not produce infectious progeny virus. The term "viable" as used in that statement is synonymous with "infectious." (See for example, Knipe Application, Page 2, lines 28-30). [Ex 1009, ¶ 9.]
>
> In my opinion, based on the overall disclosure in the Knipe application that an important property of an effective vaccine using a mutated herpes virus is preventing a spread of viral infection by preventing production of infectious virus particles, when coupled with the testing of mutants by determining whether or not the mutants produced infectious virus, indicates to one of ordinary skill in the art at the time of the filing of the Knipe Application that Knipe was in possession of an invention of a vaccine in which herpes virus is mutated to prevent the production of infectious viral progeny. [Ex 1009, ¶ 12.]
>
> Although Knipe discloses mutations in herpes virus that may prevent production of virus particles, this does not indicate to one of ordinary skill in the art that Dr. Knipe was only in possession of a vaccine in which the mutation is one that produces no virus particles. [Ex 1009, ¶ 16.]
>
> At the time of the filing of the Knipe Application a wide variety of mutated herpes viruses were known in the art. Some of such mutations prevented production of virus particles. Other mutants produced particles, that are

> not infectious. These would be mutants that are defective for the expression of any one of four essential viral glycoproteins, gB, gD, gH and gL in that they require a complementing cell line expressing the gene mutated in the virus for the production of viable virus. Therefore, such mutants are "replication defective", and one skilled in the art would understand that such mutants are part of the invention disclosed in the Knipe Application. [Ex 1009, ¶ 18.]
>
> I further note that the art still refers to replication defective herpes virus as a mutant that requires a complementary cell line for replication (see the abstract of Proc. Natl. Acad. Sci., Vol. 93, pp. 11307-11312) (Knipe Exhibit 1011).
>
> In this respect genes required for replication are listed in Table 1 (P 11308) and such gene includes the gH gene of the herpes virus. Table 1 by using the symbol "**N**" in the column headed "Dispensible in Cell Culture" indicates that virus can not be replicated unless the gene is present. [Ex 1009, ¶ 20.]
>
> What one skilled in the art would find important from the teachings of the Knipe Application with respect to mutations of the herpes virus is that there should be no spread of viral infection, whereby one skilled in the art would understand that mutants that produced particles which were not infectious (or not viable) are also part of the invention in that they would meet an important requirement set forth in the Knipe Application, i.e., the mutation prevents the production of viable progeny in the absence of a complementing cell line. [Ex 1009, ¶ 31.]

87. The Proc. Natl. Acad. Sci. article (Ex 1011) referred by Dr. DeLuca in his testimony (Ex 1009, ¶ 20) was published in October 1996 more than a year after the July 31, 1992 filing date of the Knipe '912 application.

88. Knipe submitted an amendment and response on December 23, 1997 in the '601 application [Ex 2016] arguing that the then pending claims were not anticipated by or rendered obvious over Inglis PCT application (WO 92/02563 [Ex 2016]). The amendment states:

> ...the viral mutants of both inventions [Knipe and Inglis PCT application] have the ability to enter a cell initially, and both are incapable of infecting other cells in turn. But the two inventions accomplish this in completely different ways. The mutant of Inglis et al. may infect a cell initially, can replicate its genome normally, and can package viral particles, but cannot make a protein required for the viral infection of new host cells (thereby producing non-infectious progeny).
>
> The [Knipe] mutants ... also infect a cell, but are incapable of completely replicating their genomes upon infection. Unlike the mutants of Inglis et al. they cannot create new viral particles. [Ex 20016, p. 6, l. 24 - p. 7, l. 2.]

89. In the December 23, 1997 amendment to the '601 application, Knipe had amended all of the then pending independent claims to require the mutation to occur in one or more genes encoding a protein essential for viral **genome** replication to render the herpesvirus replication defective [Ex 2016, pp. 2-4].

90. Knipe filed an amendment to the '601 application on July 24, 2000 (Ex 1005) requesting that present claim 42 be amended as follows:

> 42. (Amended) A vaccine comprising a pharmaceutically acceptable carrier and an amount of a mutant herpesvirus effective to elicit a protective immune response, said mutant herpes virus containing a genome in which a viral gene encoding a protein which is essential for production of infective virus has been deleted or inactivated, wherein said mutant virus is able to cause production of infectious new virus [particles] in a recombinant complementing host cell expressing a gene which complements said essential viral gene, but is unable to cause production of infectious new virus [particles] when said mutant virus infects a host cell other than said recombinant complementing host cell, [for prophylactic or therapeutic use in generating an immune response in a subject infected therewith].

91. The July 24, 2000 amendment (Ex 1005) accompanied Knipe preliminary motion 5 to amend and add claims (Paper 51).

92. For reasons stated above, Knipe preliminary motion 5 has been denied.

93. The Inglis PCT application (WO 92/05263, Ex 2006) was published April 2, 1992.

Inglis' position

94. According to Inglis, Knipe is relying on ambiguous language, i.e., a "replication defective" herpesvirus and statements of general goals to provide descriptive support for claims 42, 45, 47 and 48.

95. Further according to Inglis, "replication defective" herpesvirus mutants, in the context of the '912 application, are mutants that produce no progeny on normal host cells (Inglis testimony, Ex 2002, ¶¶ 17 and 24; Mocarski testimony, Ex 2024, ¶¶ 5 and 6).

96. Still further according to Inglis, since the '912 application does not provide written support for the later-added claims which read on broader embodiments wherein the mutant produce noninfectious progeny, claims 42, 45, 47 and 48 are not entitled to benefit of the July 31, 1992 filing date of the '912 application.

97. Without benefit of the '912 application, Inglis PCT application and Nguyen are citable as prior art under 35 U.S.C. § 102(b). As a result, Inglis argues that Knipe claims 42, 45, 47 and 48 are anticipated by Inglis PCT application (Ex 2006) and by Nguyen (Ex 2012) under 35 U.S.C. § 102(b). (See Paper 37, pp. 7-9 and Ex 2016 for an element-by-element comparison of Knipe claims 42, 45, 47 and 48 to the disclosures of Inglis PCT application and Nguyen.)

Discussion

Inglis preliminary motion 5, when considered in light of the evidence relied upon in support of the motion, establishes a sufficient basis for holding Knipe claims 42, 45, 47 and 48 to be unpatentable to Knipe under 35 U.S.C. § 102(b) over either Inglis PCT application (WO 92/05263, Ex 2006) or Nguyen (Ex 2012).

Since Knipe has not called our attention to any specific argument or evidence to support the separate patentability of claims 42, 45, 47 and 48 if a determination is made that they are not entitled to the filing date of the '912 application, the patentability of these claims stand or fall with their entitlement to the filing date of the '912 application.

Furthermore, to the extent Knipe argues that the Inglis PCT application, published April 2, 1992, may be prior art under 35 U.S.C. § 102(a) vis-a-vis the '912 application, filed July 31, 1992 (Paper 69, p. 13), Knipe has not submitted any meaningful evidence supporting the patentability of claims 42, 45, 27 and 48 if these claims are entitled to the benefit of the '912 application filing date.

Since the '912 application does not provide written description for later-added claims which read on broader embodiments wherein the mutants produce noninfectious progeny, Knipe claims 42, 45, 47 and 48 are not entitled to benefit under 35 U.S.C. § 120 of the July 31, 1992 filing date of the '912 application for the following reasons.

"Satisfaction of the description requirement insures that subject matter presented in the form of a claim subsequent to the filing date of the application was sufficiently disclosed at the time of filing so that the prima facie date of invention can fairly be held

to be the filing date of the application." Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991) (quoting In re Smith, 481 F.2d 910, 914, 178 USPQ 620, 623-24 (CCPA 1973)). In order to determine whether a prior application meets the "written description" requirement with respect to later-filed claims, the prior application need not describe the claimed subject matter in exactly the same terms as used in the claims; it must simply indicate to persons skilled in the art that as of the earlier date the applicant had invented what is now claimed. Id. at 1563, 19 USPQ2d at 1116. The test is whether the disclosure of the application relied on reasonably conveys to a person skilled in the art that the inventor had possession of the claimed subject matter at the time of the earlier filing. Ralston Purina Co. v. Far-Mar-Co. Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985). "Precisely how close the original description must come to comply with the description requirements of Section 112 must be determined on a case-by-case basis." Vas-Cath, 935 F.2d at 1561, 19 USPQ2d at 1116.

The issue before us then is whether or not a vaccine comprising a "replication-defective" herpesvirus as described in the '912 application is limited to mutants which, upon infecting a normal host cell, fail to produce progeny virus or to mutants which, more broadly, also include mutants which produce noninfectious progeny virus.

It may be self-evident that noninfectious progeny virus (i.e., noninfectious viral particles) cannot be produced by a mutant herpesvirus which does not produce any progeny virus upon infecting a host cell. However, our reading of the '912 application

[Ex 2009] does not reveal that Knipe described a vaccine comprising a herpesvirus mutant which can produce noninfectious viral particles upon infecting a normal host cell.

To the contrary, the '912 application expressly states that "[i]nfection will not produce progeny" (Ex 2009, p. 2, ll. 30-31). The '912 application expressly characterizes Knipe's mutant herpesviruses as being "effectively incapable of producing viable progeny virus" (Ex 2009, p. 11, ll. 11-16). Suitable candidate viruses may contain mutations in the ICP27 or ICP8 genes or in genes encoding capsid proteins (Ex 2009, p. 15, ll. 16-29). If a viral component, such as the capsid, is not produced because the gene encoding it is deleted or inactivated, then one of ordinary skill in the art would not expect progeny viral particles to be formed. Progeny virus could not be assembled because an essential viral component, the capsid, would be lacking.

Inglis also relies on the opinions of Drs. Inglis (Ex 2002, ¶ 23) and Mocarski (Ex 2024, ¶¶ 5 and 6 and Ex 2035, ¶7)) who state that a vaccine comprising a "replication-defective" herpesvirus mutant as described in the '912 application is limited to mutants which, upon infecting a normal host cell, fail to produce progeny virus. It is not a question of whether progeny virus is infectious or noninfectious. There is simply no description that progeny virus are produced.

Knipe acknowledges that the preferred mutants disclosed in the '912 application are "those that do not spread infection by preventing production of particles" (Paper 69, p. 7). However, in its opposition (Paper 69, p. 6), Knipe argues that "incapable of

producing viable progeny virus" means that the mutant virus is incapable of producing live, infectious viral progeny. Knipe relies on the opinion of Dr. DeLuca (Ex 1009, ¶¶ 4, 9, 12, 18 and 31) who states that the '912 application described mutant herpesvirus that produced noninfectious particles.

To the extent there is a conflict in the opinions of Drs. Inglis and Mocarski vis-a-vis the opinion of Dr. DeLuca, we credit the former opinions over the latter opinion. In this respect we accept the testimony of Drs. Inglis and Mocarski that a herpesvirus mutant is "viable" or "live" if it can "infect target cells in the host to be protected" without producing progeny (Ex 2009, p. 2, ll. 28-31). Infection without progeny is not interchangeable with an inability to cause production of infectious new virus.

Moreover, contrary to the DeLuca opinion, the '912 application states that the vaccine "virus elicits a protective immune repsonse [sic, response], e.g., by virally induced or encoded immunogens produced by infected cells" (Ex 2009, p. 2, ll. 31-33). In discussing glycoprotein immunogens, e.g., gH, the '912 application states "[t]hese glycoprotein immunogens may be inserted into a mutated background, e.g., ICP27 or ICP8" (Ex 2009, p. 15, ll. 26-28). Our reading of this disclosure is that the herpesvirus has a mutation in its ICP27 or ICP8 gene, not in the gH gene, and is consistent with the disclosure that "[i]nfection will not produce progeny, yet the virus elicits a protective immune response" (Ex 2009, p. 2, ll. 30-31). Furthermore, we note that the Proc. Natl. Acad. Sci. (PNAS) article (Ex 1011) referred by Dr. DeLuca in his testimony (Ex 1009, ¶ 20) was published in October 1996, some four years after the July 31, 1992 filing date

of the Knipe '912 application. Knipe has not directed our attention to where the record establishes that the PNAS article is evidence of the state of the art existing on the filing date of the '912 application. Cf. In re Glass, 492 F.2d 1228, 181 USPQ 31 (CCPA 1974) (specification has to be enabling as of its filing date) and In re Scarbrough, 500 F.2d 560, 182 USPQ 298 (CCPA 1974) (same).

In its opposition (Paper 69, p. 7), Knipe also relies on the data presented in Table 1 of the '912 application (Ex 2009, p. 28). This data involves determining whether or not a herpesvirus has been successfully mutated in its ICP27 gene. Ascertaining whether or not a deletion or inactivation mutation has occurred in the ICP27 gene of a particular herpesvirus sample by determining whether it will only grow in a complementing cell line (V27) but not a normal (Vero) cell line is not inconsistent with using mutants which, upon infecting a normal host cell, fail to produce progeny virus.

Although Knipe also argues in its opposition (Paper 69, pp. 7-8) that "replication defective" herpesvirus are not limited to mutant herpesviruses which are incapable of producing DNA, Inglis has replied that that is not its position (Paper 95, pp. 6-7). According to Inglis, the mutants are defective in genes required for genome, i.e., DNA, replication **and/or** for the expression of late viral gene products such that no progeny viral particles are produced when they infect normal host cells (See also Ex 2002, ¶ 9).

In its opposition (Paper 69, pp. 10-11), Knipe also seeks to rely on Inglis' British priority application (Ex 2001) to construe the phrase "replication defective" as used in

the '912 application to encompass mutants which produce noninfectious progeny virus. However, we agree with Dr. Mocarski's testimony that the phrase "replication defective" has some ambiguity and would be understood according to its context (Ex 2024, ¶ 5). Thus, the proper context for construing the term "replication defective" as used in the '912 application is the '912 application itself, not Inglis' British priority application.

Therefore, we find that the subject matter of Knipe claims 42, 45, 47 and 48 is not described in the '912 application as required by the first paragraph of 35 U.S.C. § 112. Claims 42, 45, 47 and 48 are not entitled to benefit under 35 U.S.C. § 120 of the July 31, 1992 filing date of the '912 application. Without benefit of the '912 application, Inglis PCT application and Nguyen are citable as prior art under 35 U.S.C. § 102(b).

It is not necessary for us to consider whether claims 42, 45, 47 and 48 are anticipated by the Inglis PCT application under 35 U.S.C. § 102(a).

20. Inglis preliminary motion 6

Inglis preliminary motion 6 (Paper 38) seeks entry of judgment under 37 CFR § 1.633(a) as to Knipe claims 1-9, 25, 26, 32-34, 36-39 and 41-48. According to Inglis, Knipe claims 1-9, 25, 26, 32-34, 37-39 and 42-48 are anticipated by Nguyen (Ex 2012) under 35 U.S.C. § 102(b). Further, according to Inglis, Knipe claims 9, 32-34, 36-39 and 41-48 are anticipated by Inglis PCT application (WO 9305263, Ex 2006) under 35 U.S.C. § 102(b). Knipe opposes (Paper 70); Inglis replies (Paper 96).

Inglis has provided an element-by-element comparison between Knipe claims 1-9, 25, 26, 32-34, 36-39 and 41-48 and the disclosures of Inglis PCT

application and Nguyen (see Facts 56 and 58 above).

98. Knipe claims 1-8, 25 and 26 have been held unpatentable under 35 U.S.C. § 102(b) as anticipated by Nguyen. See Inglis preliminary motion 4 supra.

99. Knipe claims 42, 45, 47 and 48 have been held unpatentable under 35 U.S.C. § 102(b) as anticipated by Nguyen. See Inglis preliminary motion 5 supra.

Therefore, Inglis preliminary motion 6 is dismissed as moot as to Knipe claims 1-8, 25, 26, 42, 45, 47 and 48.

As to the remaining claims, Inglis preliminary motion 6, when considered in light of the evidence relied upon in support thereof, establishes a sufficient basis for holding Knipe claims 9, 32-34, 37-39, 43, 44 and 46 and Knipe claims 9, 32-34, 36-39, 41, 43, 44 and 46 to be unpatentable under 35 U.S.C. § 102 over Nguyen and Inglis PCT application, respectively.

Knipe seems to concede that Inglis PCT application anticipates claims 9, 32-34, 36-39, 41, 43, 44 and 46 and that Nguyen anticipate claims 9, 32-34, 37-39, 43, 44 and 46 under 35 U.S.C. § 102(b) if these claims are not accorded benefit of the July 31, 1992 filing date of the '912 grandparent application (Paper 70). Accordingly, the dispositive issue is whether Knipe claims 9, 32-34, 36-39, 41, 43, 44 and 46 are entitled to benefit under 35 U.S.C. § 120 of the July 31, 1992 filing date of the '912 application.

100. Knipe admits that (See Paper 70, p. 3 where Knipe admits Inglis facts 10, 12 and 13 stated in Paper 38, pp. 5-6):

a) The Inglis PCT application and Nguyen, taken separately, each contain

disclosures expressly showing features providing each and every element required by Knipe claims 9, 32-34, 37-39, 43, 44 and 46. [Inglis fact 10.]

* * * * *

b) Each and every element required by Knipe claims 36 and 41 (dependent on claims 32 and 37, respectively) is satisfied by the disclosure of Inglis PCT application. [Inglis fact 12.]

* * * * *

c) Nguyen discloses three specific embodiments falling within Knipe claims 9, 32-34, 37-39, 43, 44 and 46, namely vaccines based on HSV-1 herpesvirus mutants d120, d301 and n504 and their use. [Inglis fact 13.]

101. The '912 application (Ex 2009) discloses:

a) The majority of virus-specific products responsible for eliciting a protective immune response are proteins and glycoproteins which are expressed in the infected cell and generally can be found on the surface of the virion [p. 12, ll. 26-29].

* * * * *

b) Mutating HSV-1 ICP8, ICP24 and ICP4 genes by known techniques generated replication defective herpesvirus mutants d301, n504 and d120, respectively [p. 16, ll. 22-30].

* * * * *

c) Figure 1 graphically depicts the amounts of HSV-1 specific antibodies produced by mice after inoculation with wild-type HSV-1 (KOS) and the herpesvirus

mutants d120, d301 and n504 in comparison with an uninfected control [p. 4, ll. 1-13 and p.19, ll. 10-34].

* * * * *

d). Figure 2 graphically depicts the HSV-1 specific T cell-mediated activity produced in mice after inoculation with wild-type HSV-1 (KOS) and the herpesvirus mutants d120, d301 and n504 in comparison with an uninfected or non-HSV-1 control [p. 4, ll. 14-23 and p. 19, l. 31 - p. 20, l. 20].

* * * * *

e) Figure 3 graphically depicts the survival of mice inoculated with the herpesvirus mutants d120, d301 and n504 that were subsequently challenged with wild-type virus [p. 4, l. 24 - p. 5, l. 5 and p. 20, l. 21 - p. 21, l.9].

102. Knipe claims 9, 36, 43, 44 and 46 claim a vaccine based on replication defective herpesvirus. Knipe claims 43 and 44 recite that the vaccine is for "prophylactic or therapeutic use". Knipe claims 32-34, 37, 39 and 41 claim a method of immunizing or inducing an immune response in a mammal using a vaccine comprising replication defective mutant herpesvirus.

Inglis' position

103. According to Inglis, Knipe claims 9, 32-34, 36-39, 41, 43, 44 and 46 are not entitled to benefit under 35 U.S.C. § 120 of the July 31, 1992 filing date of Knipe grandparent application '912 because the '912 application only describes a restricted subset of replication defective mutant herpesvirus vaccines which are mutated in an

essential gene required for the formation of viral progeny (Paper 38, pp. 3 and 7; Inglis testimony Ex 2002, ¶ 23).

104. Further according to Inglis, the restricted subset of replication defective mutant herpesvirus vaccines that is described in the '912 application expressly excludes results with the ICP4 mutant d120 as part of the invention at page 4, lines 1-4 (Paper 38, p. 7). This exclusion was removed in Knipe' s continuation-in-part applications, the '106 application (Ex 2010, p. 4, description of Figure 1) and the 601 application (Ex 2011, p. 4, description of Figure 1).

105. Still further according to Inglis, the '912 application discloses vaccines for prevention of viral disease but does not mention the use of vaccines to treat previously acquired viral disease.

106. Without benefit of the '912 application, Inglis PCT application and Nguyen are citable as prior art under 35 U.S.C. § 102(b). As a result, Inglis argues that Knipe claims 9, 32-34, 36-39, 41, 43, 44 and 46 are anticipated by Inglis PCT application and are, therefore, unpatentable under 35 U.S.C. § 102(b). Inglis further argues that Knipe claims 9, 32-34, 37-39, 43, 44 and 46 are anticipated by Nguyen and are, therefore, unpatentable under 35 U.S.C. § 102(b).

Discussion

A movant bears the burden of establishing its entitlement to the relief sought by a preponderance of evidence. 37 CFR § 1.637(g). A movant, however, is not obliged to anticipate all grounds for opposition and meet them is its motion. Cf. U.S. Patent &

Trademark Off., "Interference Practice - Interference Rules Which Require a Party to 'Show the Patentability' of a Claim", 1217 Off. Gaz. 17 (November 8, 1988) (normally requiring movant only to show compliance with the written description of 35 U.S.C. § 112, first paragraph).

Here, the dispositive issue in Inglis preliminary motion 6 is whether or not the subject matter of Knipe claims 9, 32-34, 36-39, 41, 43, 44 and 46 is described in Knipe's '912 application as required by the first paragraph of § 112 so as to be entitled to benefit of the July 31, 1992 filing date of the '912 application under 35 U.S.C. § 120.

For the reasons stated in the above discussion of Inglis preliminary motion 5, in our view the '912 application does not describe vaccines and uses comprising an unrestricted genus of replication defective herpesvirus mutants as recited in Knipe claims 9, 32-34, 36-39, 41, 43, 44 and 46. It is our view, for reasons stated in the above discussion of Inglis preliminary motion 5, that Inglis has established that the '912 application is limited to vaccines and uses comprising "replication defective" herpesvirus mutants which, upon infecting a normal host cell, fail to produce progeny virus. Since Knipe claims 9, 32-34, 36-39, 41, 43, 44 and 46 are not limited to vaccines and uses comprising herpesvirus mutants which fail to produce progeny virus upon infecting a normal host cell, these claims are not entitled to benefit of the July 31, 1992 filing date of the '912 application under 35 U.S.C. § 120.

It is not necessary for us to decide whether or not vaccines comprising herpesvirus mutant d120 are part of the restricted genus of replication defective

herpesvirus mutants disclosed in the '912 application because Knipe claims 9, 32-34, 36-39, 41, 43, 44 and 46 are not limited to vaccines comprising this restricted genus of replication defective herpesvirus mutants.

Additionally, Inglis urges that the '912 application does not disclose treatment of a previously existing disease, i.e., therapeutic treatment, as required by Knipe claims 42-44.

107. Knipe claims 43 and 44 require vaccines "for prophylactic or therapeutic use in generating an immune response in a subject infected therewith [herpesvirus]".

108. Knipe admits that prophylactic treatment is well known to mean prevention, whereas therapeutic use means treatment of previously acquired disease. (See Paper 70, p. 2 where Knipe partially admits Inglis fact 5 set forth in Paper 38, p. 4.[11])

In its opposition (Paper 70, p. 5), Knipe argues that "Page 3, lines 2 and 3 of the '912 application, 'subsequent infection by wild-type virus is prevented or is less severe in terms of duration and extent.'" provides support for treating herpesvirus infection as defined in claims 43 and 44.

While Knipe admits that prophylactic treatment is different from therapeutic treatment, i.e., treatment of subsequent infection is different from treatment of an

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[11] Inglis fact 5 a) reads in relevant part: "It is also notable that claims 42-44 recite that the vaccine is for 'prophylactic or therapeutic use', where phrophylaxis is well known to mean prevention, while therapy in this context means treatment of previously required disease. [Paper 70, p. 4.]

Knipe (Paper 70, p. 2) states "[t]he Party Knipe denies Inglis Fact 5 to the extent that in an amendment filed on July 24, 2000 (Knipe Exhibit 1005), the Party Knipe deleted the language 'for prophylactic or therapeutic use in generating an immune response in a subject infected therewith' from Claim 42."

existing infection (see Fact 108), Knipe has not shown that treatment of subsequent infection provides a reasonable expectation that that same treatment will cure or lessen the duration and extent of an existing infection. Therefore, in our view, the '912 application reasonably conveys to one skilled in the art that Knipe may have been in possession of a restricted genus of vaccines comprising replication defective herpesvirus mutants useful for prophylactic treatment of subsequent herpes virus infection, but not therapeutic treatment of existing infection. For this additional reason, Knipe claims 43 and 44 are not entitled to benefit of the July 31, 1992 filing date of the '912 application under 35 U.S.C. § 120.

We find that the subject matter of Knipe claims 9, 32-34, 36-39, 41, 43, 44 and 46 is not described in the '912 application as required by 35 U.S.C. § 112, first paragraph, and, therefore, these claims are not entitled to benefit of the July 31, 1992 filing date of the '912 application under 35 U.S.C. § 120. Without benefit of the filing date of the '912 application, Inglis PCT application and Nguyen are citable as prior art under 35 U.S.C. § 102(b) as to Knipe claims 9, 32-34, 36-39, 41, 43, 44 and 46.

Because we grant Inglis preliminary motion 6 with respect to § 102(b), it is not necessary for us to consider whether Knipe claims 9, 32-34, 36-39 and 41-48 are anticipated by Inglis PCT application under 35 U.S.C. § 102(a). Therefore, Inglis preliminary motion 6 is granted as to Knipe claims 1-9, 25, 26, 32-34, 37-39 and 42-48. As to Knipe claims 36 and 41, Inglis preliminary motion 6 is dismissed since Knipe claims 36 and 41 have been designated as not corresponding to Count 2 and therefore

no longer involved in this interference. However, based upon the findings and analysis above, we exercise our discretion under 37 CFR § 1.659(a) and enter a recommendation that Knipe claims 31 and 41 be rejected as anticipated by Inglis PCT application (Ex 2006) under 35 U.S.C. § 102(b).

21. **Inglis preliminary motion 1**

Inglis moves pursuant to 37 CFR § 1.633(f) for benefit for the purpose of priority of the September 23, 1991 international filing date of Inglis' PCT application (Ex 2006) in this interference (Paper 33).

Inglis preliminary motion 1, when considered in light of the evidence relied upon in support of the motion, establishes a sufficient basis for granting Inglis benefit of the September 23, 1991 filing date of Inglis' PCT application for purposes of priority. Further, Knipe has not opposed Inglis preliminary motion 1. Therefore, Inglis preliminary motion 1 is granted.

22. **Inglis preliminary motion 2**

Inglis moves pursuant to 37 CFR § 1.633(f) for benefit for the purposes of priority of the September 25, 1990 filing date of Inglis' U.K. Application 9020799.4 (the '799 application, Ex 2001) (Paper 34). Knipe opposes (Paper 66); Inglis replies (Paper 92).

109. Knipe admits that the NOTICE DECLARING INTERFERENCE has accorded Inglis benefit of U.S. application 08/030,073. [See Paper 66, p. 2 where Knipe admits Inglis Fact 1 in Paper 34, p. 2.]

110. Knipe admits that U.S. application 08/030,073 is a 35 U.S.C. § 371 national phase of Inglis' international application PCT/GB91/01632[12] (Inglis PCT application). [See Paper 66, p. 2 where Knipe admits Inglis Fact 2 in Paper 34, p. 2.]

111. Knipe admits Inglis PCT application claims priority from the '799 application, but denies that Inglis is entitled to benefit of the '799 application. [See Paper 66, p. 2 where Knipe partially admits Inglis Fact 3 in Paper 34, p. 2.]

112. Knipe admits that claim 1 of Inglis' U.S. patent 5,665,362 ('the '362 patent) is one of the claims which, in the alternative, forms part of the present count. [See Paper 66, p. 2 where Knipe admits Inglis Fact 4 in Paper 34, pp. 2-3.]

113. Knipe admits that the '799 application describes each element of Inglis '362 claim 1. [See Paper 66, p. 2 where Knipe admits Inglis Fact 5 in Paper 34, pp. 3-5.]

114. Knipe admits that the '799 application describes a specific embodiment within Inglis '362 claim 1, i.e., a vaccine comprising a herpesvirus mutated by inactivating its gH gene. [See Paper 66, p. 2 where Knipe admits Inglis Fact 6 in Paper 34, p. 5.]

115. The '799 application discloses (Ex 2001, p. 1, ll. 3-3-7) that

> [t]he present invention relates to viral vaccines. In particular, it relates to genetically engineered attenuated viruses for use as vaccines; vaccines comprising the attenuate[d] viruses; recombinant cell line; and to methods relating to the production of vaccines.

116. Dr. Stephen C. Inglis testified on behalf of Inglis (Ex 2002, ¶¶ 43 and 44) that:

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[12] Inglis' international application PCT/GB91/01632 published as WO 92/05263 (see Ex 2006).

A scientist of average ability, working from the disclosure of '799, could make the gH mutant herpesvirus vaccine which is described. In 1990, a person working in the field of recombinant viral vaccines would have held a degree in virology or molecular biology or a related discipline and would have had experience with genetically engineered virus mutants and in making and testing viral vaccines. '799 contains detailed literature citations, showing that the necessary genetic manipulations for making virus mutants that we disclosed as suitable for these vaccines were conventional in the art at that time. '799 makes clear that the materials and methods needed to make the gH mutant herpesvirus vaccine (as well as other embodiments using different genes known to be 'essential') were known and available in 1990. Only a limited amount of experimental work would have been needed to make the vaccines described in '799. [Ex 2002, ¶ 43.]

The '799 application refers to conventional, recognized techniques for administering viral vaccines and animal models for assessing their efficacy. The disclosure is aimed at a reader having some background with the animal models used to assess viral vaccines. See '799, page 19, line 21 - page 21, line 3. Some other types of mutant or attenuated herpes viruses were previously known as vaccines, thus the techniques for administering them and establishing dose were in themselves well-known in the field and would readily have been used. [Ex 2002, ¶ 44.]

117. The '799 application states that:

For herpes simplex virus, cell lines expressing the gB glycoprotein (Cai et al, J. Virol. 62, 714-721, 1987) and the Immediate Early protein ICP4 (Deluca et al., J. Virol., 56, 558, 1985) have been produced, and these have been shown capable of supporting the replication of viruses with specifically inactivated copies of the corresponding genes. [Ex 2001, p. 4, ll. 18-24.]

* * * * *

All genetic manipulation procedures are carried out according to standard methods described in "Molecular Cloning", A Laboratory Manual, eds. Sambrook, Fritsch and Maniatis, Cold Spring Harbor Laboratory Press, 1989. [Ex 2001, p. 14, ll. 2-5.]

* * * * *

A vaccine comprising the attenuated [mutant herpes] virus can be prepared and used according to standard techniques known in the art. For example, the vaccine may also comprise one or more excipients

and/or adjuvants. The effective dose of attenuated virus to be provided by the vaccine may be determined according [to] techniques well known in the art. [Ex 2001, p. 20, ll. 24-26.]

118. The '799 application describes

a) production of a cell line expressing the herpesvirus gH gene, including literature citations to described techniques (Ex 2001, pp. 14-15);

b) production of a herpesvirus having an inactivated gH gene, including literature citations to described techniques (Ex 2001, pp. 16-20); and,

c) an animal model for testing immune response to the gH inactivated herpesvirus mutant and its ability to protect against infection by wild-type herpesvirus, including literature citations to described techniques (Ex 2001, pp. 19-21).

Inglis' position

119. According to Inglis, a vaccine based on a gH mutant herpesvirus is fully described and enabled by the '799 application.

120. Further, according to Inglis, this gH mutant herpesvirus vaccine is a constructive reduction to practice of count 1.

121. Still further according to Inglis, the gH mutant herpesvirus embodiment is described in substantially the same way in the '799 application and the Inglis' involved '362 patent (Paper 34, Fact 11, pp. 7-9).

Discussion

A party may be accorded benefit for the purposes of priority of an earlier

application, if the earlier application contains an enabling description of a single embodiment within the scope of the count. Hunt v. Treppschuh, 523 F.2d 1386, 1389, 187 USPQ 426, 429 (CCPA 1975) (an application need only disclose a single enabled embodiment within the scope of the count to constitute a constructive reduction to practice of the invention of the count); See also Weil v. Fritz, 572 F.2d 856, 865 n.16, 196 USPQ 600, 608 n.16 (CCPA 1978) (as Hunt v. Treppschuh *** explains, "the § 112 paragraph, requirements need only be met for an embodiment within the count" where the count is drawn to a genus and the previously-filed application discloses only a species thereof).

In its opposition (Paper 66, p. 6, ¶ 1), Knipe argues that

> [a]t best, the Inglis United Kingdom Application No. 9020799.4 provides prophetic guidance regarding the construction of a mutant Herpes virus which cannot produce infectious new viral particles in the absence of a complementing cell, and the use of such a mutant Herpes virus in a vaccine. Thus, the Inglis United Kingdom '799 application does not include sufficient information whereby one skilled in the art would conclude that as of such time Inglis was in possession of the invention as defined by the Count, and fails to fulfill the description requirements of 35 U.S.C. 112.

Even assuming the '799 application taught how to make the required mutant herpesvirus, Knipe further argues that the '799 application provides no guidance as to formulating the mutant herpesvirus into a vaccine or how to determine an effective immunizing amount as required by the count (Paper 66, p. 6, ¶ 3).

The first paragraph of 35 U.S.C. § 112 requires nothing more than objective enablement. In re Marzocchi, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA

1971). In satisfying the enablement requirement, an application need not teach, and preferably omits, that which is well-known in the art. Hybritech, Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).

Here, the '799 application provides detailed, literature-referenced guidance for making a gH mutant herpesvirus (Ex 2005, pp. 14-19). The '799 application provides detailed, literature-referenced guidance for assessing the ability of a gH mutant herpesvirus vaccine to protect against wild-type virus challenge (Ex 2005, pp. 19-20). Furthermore, there is testimony from Dr. Inglis that the procedures used in the '799 application were within the ordinary skill in the art (Ex 2002, ¶¶ 43 and 44). This testimony, which we find credible, stands unrebutted by Knipe. Knipe has not provided meaningful evidence or directed our attention to where in the record evidence is found challenging Inglis' position that only well known, conventional genetic techniques as reflected in the literature cited in the '799 application are required to make and use the invention of the count. Knipe's attorney arguments are not evidence of nonenablement or lack of adequate written description.

Accordingly, we conclude that Inglis has met its burden of making out a prima facie case of enablement.

"The function of the description requirement [of the first paragraph of 35 U.S.C. 112] is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him." In re Wertheim, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). "It is not necessary that

the application describe the claim limitations exactly, ... but only so clearly that persons of ordinary skill in the art will recognize from the disclosure that appellants invented the processes including those limitations." Wertheim, 541 F.2d at 262, 191 USPQ at 96 citing In re Smythe, 480 F.2d 1376, 1382, 178 USPQ 279, 284 (CCPA 1973).

Here, the '799 application describes genetically engineered attenuated viruses, i.e., gH mutant herpesvirus, vaccines comprising the gH mutant herpesvirus, complementing recombinant cell lines, methods relating to the production of mutant herpesvirus vaccines and methods relating to testing the efficacy of mutant herpesvirus vaccines. Thus, we find that the disclosure in the '799 application would have reasonably conveyed to one of ordinary skill in the art that Inglis possessed an embodiment within the scope of the count, i.e., a gH mutant herpesvirus vaccine.

Therefore, based upon the foregoing, we conclude that Inglis is entitled to benefit for the purpose of priority of the '799 application, having shown a prior constructive reduction to practice of an embodiment, i.e., the gH mutant herpesvirus vaccine, within the subject matter of the count.

23. Inglis preliminary motion 3

Inglis moves pursuant to 37 CFR § 1.633(f) for benefit for the purpose of priority of the March 8, 1991 filing date of Inglis' U.K. Patent Application 9104903.1 (the '903 application, Ex 2005) (Paper 35). Knipe opposes (Paper 67); Inglis replies (Paper 93).

122. Knipe admits that PCT/GB91/01632 claims priority from Inglis U.K. application 9104903.1 (the '903 application). [See Paper 67, p. 2 where Knipe admits

Inglis Fact 3 in Paper 35, p. 2 insofar as PCT/GB91/01632 makes a claim for priority to the '903 application.]

123. Knipe admits that the '903 application describes each element of Inglis '362 claim 1. [See Paper 67, p. 2 where Knipe admits Inglis Fact 5 in Paper 35, pp. 3-4.]

124. Knipe admits that the '903 application describes a specific embodiment within Inglis '362 claim 1, i.e., a vaccine comprising a herpesvirus mutated by inactivating its gH gene. [See Paper 67, p. 2 where Knipe admits Inglis Fact 6 in Paper 35, p. 5.]

125. Dr. Stephen C. Inglis testified on behalf of Inglis (Ex 2002, ¶ 46) that:

> I have also reviewed our second patent application filed in the UK, no. GB9104903.1, filed 8 March 1991 (Ex 2005; "'903"). '903 contains all of the disclosure of '799 as discussed above, and additionally provides results from experiments in animals in the passage between page 19, line 19 and page 22, line 71) showing induction of protective immunity in an animal model.

126. The '903 application describes vaccinating mice with heat killed gH mutant herpesvirus (groups a and b) and live gH mutant herpesvirus (groups c and d). After 14 days the mice were challenged with (i.e., exposed to) wild-type herpesvirus (SC16). The mice inoculated with live gH mutant herpesvirus vaccine are said to have had reduced titers of wild-type herpesvirus in their ears and no wild-type herpesvirus in their cervical ganglia compared to mice inoculated with killed virus vaccine. [Ex 2005, pp. 19-22.]

Inglis' position

127. According to Inglis, a vaccine based on a gH mutant herpesvirus is fully

described and enabled by the '903 application.

128. Further according to Inglis, this gH mutant herpesvirus vaccine is a constructive reduction to practice of count 1.

129. Still further according to Ingiis, the gH mutant herpesvirus embodiment is described in substantially the same way in the '903 application and the Inglis' involved '362 patent (Paper 35, Fact 11, pp. 6-8). Moreover, according to Inglis, the '903 application provides a working example which demonstrated the efficacy of a gH mutant herpesvirus vaccine in an animal model, citing Ex 2005, p. 21, Table 1.

Discussion

The arguments and position of the parties regarding Inglis preliminary motion 3 are similar, if not essentially identical, to those presented above regarding Inglis preliminary motion 2. The difference is additional arguments based on the working example in the '903 application (Ex 2005, pp. 19-22).

In its additional opposition (Paper 67, pp. 5-7), Knipe argues that the '903 data (Ex 2005, pp. 19-22) shows an ineffective vaccine because herpesvirus was detected in the ears of the mice inoculated with gH mutant herpesvirus vaccine. Knipe further argues that the vaccination experiment lacked a control group. Knipe also argues that there is no evidence of protective immunity compared to a control, e.g., the "survival" of vaccinated mice as compared to an unvaccinated control. Therefore, Knipe argues, the '903 only describes an incomplete invention and Inglis was not yet in possession of the invention of the count.

However, Knipe has failed to provide meaningful evidence that the animal model used in the '903 application is an irrelevant model or that evidence of "survival" of vaccinated mice as compared to unvaccinated mice is the only acceptable evidence of efficacy of vaccination. While the data in the '903 application (Ex 2005, pp. 19-22) does describe the presence of wild-type herpesvirus in their ears in mice inoculated with live gH mutant herpesvirus vaccine compared to mice inoculated with killed virus vaccine, according to the data, there is no evidence of infection in the mice's cervical ganglia. Moreover, according to the data, increasing the amount of gH mutant herpesvirus in the vaccine decreased the amount of herpesvirus in the ear. Knipe has not provided meaningful evidence that one of ordinary skill in the art would not have expected further increases in the amount of live gH mutant herpesvirus in the vaccine to provide further protection.

Enablement is not precluded by the necessity for some further routine experimentation, such as determining optimal dosage amounts of vaccine. Knipe has not challenged Inglis' testimony, which we find credible, that techniques for determining effective dosages were well-known and within ordinary skill in the art (Ex 2002, ¶ 44).

Further, as pointed out by Inglis in its reply (Paper 93, p. 8 and Fact 5 on p. 3), the '903 application did use a control, i.e., mice inoculated with heat killed gH mutant herpesvirus vaccine.

We are, therefore, unpersuaded by Knipe's additional arguments that the '903 application fails to satisfy the requirements of 35 U.S.C. § 112, first paragraph.

Based on the foregoing in addition to the reasons set forth in Inglis preliminary motion 2, we conclude that Inglis is entitled to benefit for the purpose of priority of the '903 application.

E. Order

1. Inglis preliminary motion 8

Upon consideration of Inglis preliminary motion 8, and for the reasons given, it is

ORDERED that Inglis preliminary motion 8 is granted.

2. Inglis miscellaneous motion 11

Upon consideration of Inglis preliminary motion 8, it is

ORDERED that Inglis preliminary motion 11 is dismissed without prejudice to further proceedings before the primary examiner. 37 CFR § 1.604.

3. Inglis preliminary motion 12

Upon consideration of Inglis preliminary motion 12 to add Inglis count 2 to the interference, and for the reasons given, it is

ORDERED that Inglis preliminary motion 12 is dismissed without prejudice to further proceedings before the primary examiner and/or Inglis seeking an additional interference. 37 CFR § 1.604.

4. Knipe miscellaneous motion 3

Upon consideration of Knipe miscellaneous motion 3, and for the reasons given, it is

ORDERED that Knipe miscellaneous motion 3 is dismissed without prejudice to Knipe seeking an additional interference before the primary examiner. 37 CFR § 1.604.

5. Knipe miscellaneous motion 4

Upon consideration of Knipe miscellaneous motion 4, and for the reasons given, it is

ORDERED that Knipe miscellaneous motion 4 is dismissed without prejudice to Knipe seeking an additional interference before the primary examiner. 37 CFR § 1.604.

6. Knipe preliminary motion 9

Upon consideration of Knipe preliminary motion 9, it is

ORDERED that Knipe preliminary motion 9 is dismissed as moot.

7. Inglis miscellaneous motion 15

Upon consideration of Inglis miscellaneous motion 15, and for the reasons given, it is

ORDERED that Inglis miscellaneous motion 15 is dismissed as moot.

8. Inglis preliminary motion 14

Upon consideration of Inglis preliminary motion 14, and for the reasons given, it is

ORDERED that Inglis preliminary motion 14 is dismissed as moot.

9. Inglis preliminary motion 9

Upon consideration of Inglis preliminary motion 9, and for the reasons given, it is

ORDERED that Inglis preliminary motion 9 is denied.

10. Inglis preliminary motion 10

Upon consideration of Inglis preliminary motion 10, and for the reasons given, it is

ORDERED that Inglis preliminary motion 10 is denied.

11. Knipe preliminary motion 5

Upon consideration of Knipe preliminary motion 5 (Paper 51), and for the reasons given, it is

ORDERED that Knipe preliminary motion 5 is denied.

12. Knipe preliminary motion 1

Upon consideration of Knipe preliminary motion 1 to substitute Knipe proposed count 1 for the present count, it is

ORDERED that Knipe preliminary motion 1 is granted to the extent that Knipe claims 12-22 are not designated as corresponding to Count 2.

13. Knipe preliminary motion 2

Upon consideration of Knipe preliminary motion 2, it is

ORDERED that Knipe preliminary motion 2 is dismissed as moot.

FURTHER ORDERED that nothing herein shall be construed as a decision on the merits of Knipe preliminary motion 2.

14. Inglis preliminary motion 13

Upon consideration of Inglis preliminary motion 13, it is

ORDERED that Inglis preliminary motion 13 is dismissed as moot.

FURTHER ORDERED that nothing herein shall be construed as a decision on the merits of Inglis preliminary motion 13.

15. **Knipe preliminary motion 6**

Upon consideration of Knipe preliminary motion 6, it is

ORDERED that Knipe preliminary motion 6 is dismissed as moot in view of our denial of Knipe preliminary motion 5 denying entry of Knipe's proposed amendment and our disposition of Knipe preliminary motion 1.

16. **Knipe preliminary motion 7**

Upon consideration of Knipe preliminary motion 7, it is

ORDERED that Knipe preliminary motion 7 is dismissed as moot.

FURTHER ORDERED that nothing herein shall be construed as a decision on the merits of Knipe preliminary motion 7.

17. **Inglis preliminary motion 7**

Upon consideration of Inglis preliminary motion 7 (Paper 39), and for the reasons given, it is

ORDERED that Inglis preliminary motion 7 is dismissed as moot.

18. **Inglis preliminary motion 4**

Upon consideration of Inglis preliminary motion 4 (Paper 36), and for the reasons given, it is

ORDERED that Inglis preliminary motion 4 is granted.

FURTHER ORDERED that Knipe claims 1-8, 25-27 and 29 are anticipated and, therefore, unpatentable to Knipe. 35 U.S.C. § 102(b).

19. Inglis preliminary motion 5

Upon consideration of Inglis preliminary motion 5 (Paper 37), and for the reasons given it is

ORDERED that Inglis preliminary motion 5 is granted as to Knipe claims 42, 45, 47 and 48.

FURTHER ORDERED that Knipe claims 42, 45, 47 and 48 are not entitled to benefit under 35 U.S.C. § 120 of the July 31, 1992 filing date of the '912 application.

FURTHER ORDERED that Knipe claims 42, 45, 47 and 48 are anticipated and, therefore, unpatentable. 35 U.S.C. § 102(b).

20. Inglis preliminary motion 6

Upon consideration of Inglis preliminary motion 6 (Paper 38), and for the reasons given, it is

ORDERED that Inglis preliminary motion 6 is dismissed as moot as to Knipe claims 1-8, 25, 26, 36, 41, 42, 45, 47 and 48, and granted as to Knipe claims 9, 32-34, 37-39, 43, 44 and 46.

FURTHER ORDERED that Knipe claims 9, 32-34, 37-39, 41, 43, 44 and 46 are not entitled to benefit under 35 U.S.C. § 120 of the July 31, 1992 filing date of the '912 application.

FURTHER ORDERED that Knipe claims 9, 32-34, 37-39, 43, 44 and 46 are anticipated and, therefore, unpatentable. 35 U.S.C. § 102(b).

21. Inglis preliminary motion 1

Upon consideration of Inglis preliminary motion 1 (Paper 33) and for the reasons given, it is

ORDERED that Inglis preliminary motion 1 is granted.

FURTHER ORDERED that Inglis is entitled benefit for purpose of priority of Inglis' PCT application (Ex 2006).

22. Inglis preliminary motion 2

Upon consideration of Inglis preliminary motion 2 (Paper 34), and for the reasons given, it is

ORDERED that Inglis preliminary motion 2 is granted.

FURTHER ORDER that Inglis is entitled to benefit for the purpose of priority of Inglis U.K. application 9020799.4 (Ex 2001)

23. Inglis preliminary motion 3

Upon consideration of Inglis preliminary motion 3 (Paper 35), and for the reasons given, it is

ORDERED that Inglis preliminary motion 3 is granted.

FURTHER ORDER that Inglis is entitled to benefit for the purpose of priority of Inglis U.K. application 9104903.1 (Ex 2005).

M.K

FRED E. McKELVEY, Senior)
Administrative Patent Judge)
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Administrative Patent Judge) APPEALS AND
) INTERFERENCES
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Enc.:

Reference Appendix

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